# OUTCOME OF MICROBIOLOGICALLY CULTURE POSITIVE ARTHROPLASTY INFECTIONS

Dissertation submitted to the Tamil Nadu Dr. M.G.R Medical University in partial
fulfillment of the requirement for the M.S Degree Examination

Branch II (Orthopaedic Surgery)
May 2018

# OUTCOME OF MICROBIOLOGICALLY CULTURE POSITIVE ARTHROPLASTY INFECTIONS

# CERTIFICATE

This is to certify that the dissertation titled **"OUTCOME OF MICROBIOLOGICALLY CULTURE POSITIVE ARTHROPLASTY INFECTIONS"** is a bonafide work of **Dr. NIRVIN PAUL**, in the Department of Orthopaedic Surgery, Christian Medical College and Hospital, Vellore in partial fulfillment of the rules and regulations Of the Tamil Nadu Dr. M.G.R Medical University for the award of M.S Degree Branch II (Orthopaedic Surgery), under the supervision and guidance of **Prof. Dr. ALFRED JOB DANIEL** during the period of his post-graduate study from April 2015 to May 2018.

This consolidated report presented herein is based on bonafide cases, studied by the candidate himself.

**GUIDE:**
**Prof. Dr. ALFRED JOB DANIEL**,
D.Orth, M.S.Orth, Dip.N.B.
Professor of Orthopaedics,
Orthopaedics Unit –III,
Department of Orthopaedic Surgery,
Christian Medical College and Hospital,Vellore.

# CERTIFICATE

This is to certify that the dissertation titled **"OUTCOME OF MICROBIOLOGICALLY CULTURE POSITIVE ARTHROPLASTY INFECTIONS"** is a bonafide work of **Dr. NIRVIN PAUL**, in the Department of Orthopaedic Surgery, Christian Medical College and Hospital, Vellore in partial fulfillment of the rules and regulations Of the Tamil Nadu Dr. M.G.R Medical University for the award of M.S Degree Branch II (Orthopaedic Surgery), under the supervision and guidance of **Prof. Dr. ALFRED JOB DANIEL** during the period of his post-graduate study from April 2015 to May 2018.

This consolidated report presented herein is based on bonafide cases, studied by the candidate himself.

**HEAD OF THE DEPARTMENT:**
**Prof. Dr. V.T.K. TITUS**,
D.Orth, M.S.Orth, Dip.N.B.
Professor & Head,
Department of Orthopaedics,
Christian Medical College,Vellore

# CERTIFICATE

This is to certify that the dissertation titled **"OUTCOME OF MICROBIOLOGICALLY CULTURE POSITIVE ARTHROPLASTY INFECTIONS"** is a bonafide work of **Dr. NIRVIN PAUL**, in the Department of Orthopaedic Surgery, Christian Medical College and Hospital, Vellore in partial fulfillment of the rules and regulations Of the Tamil Nadu Dr. M.G.R Medical University for the award of M.S Degree Branch II (Orthopaedic Surgery), under the supervision and guidance of **Prof. Dr. ALFRED JOB DANIEL** during the period of his post-graduate study from April 2015 to May 2018.

This consolidated report presented herein is based on bonafide cases, studied by the candidate himself.

**PRINCIPAL:**
**Dr. Anna Pulimood**,
Principal,
Christian Medical College,Vellore

# DECLARATION

I hereby declare that this dissertation titled "OUTCOME OF MICROBIOLOGICALLY CULTURE POSITIVE ARTHROPLASTY INFECTIONS" was prepared by me in partial fulfillment of the regulations for the award of the M.S Degree (Final) Branch II (Orthopaedic Surgery) of the Tamil Nadu Dr. M.G.R Medical University, Chennai towards examination to be held in May 2018. This has not formed the basis for the reward of any degree to me before and I have not submitted this to any other university
previously.

**Dr. Nirvin Paul,**
Post Graduate Registrar (M.S Orthopaedics),
Department of Orthopaedics,
Christian Medical College - Vellore,
Vellore-632002

URKUND

# Urkund Analysis Result

**Analysed Document:** THESIS.docx (D31287576)
**Submitted:** 10/13/2017 12:28:00 PM
**Submitted By:** nirvin.257@gmail.com
**Significance:** 0 %

Sources included in the report:

Instances where selected sources appear:

0

# ACKNOWLEDGEMENTS

I wish to express my sincere gratitude to my guide and mentor Dr. Alfred Job Daniel, Professor of Orthopaedics, for enabling me to choose and analyze a topic that is of significant clinical value and is a challenge to the present and future generations of Orthopaedic Surgeons. I would like to thank Sir for all the help and support that was extended to me during my entire stay in CMC.

I would like to express my sincere gratitude and utmost reverence to my co guide and mentor Dr. P.R.J.V.C Boopalan, Professor of Orthopaedics, for all the help and guidance towards my dissertation. I would be eternally indebted to Sir for his constant encouragement and steadfast support during my study and also for being an excellent teacher.

I wish to express my sincere gratitude to my co guides Dr. John Antony Jude Prakash, Professor of Microbiology and Dr. V. Balaji, Professor of Microbiology, for their help in identifying patients and for all the expert advice and guidance regarding organisms causing Prosthetic Joint Infections.

I sincerely acknowledge the help rendered by Mr. Brijesh Yadav, Department of Biostatistics in performing the statistical analysis of the data and for sharing his insights into statistical methods for carrying out future studies.

I am eternally grateful to all my teachers for the guidance and encouragement throughout my entire Post graduate program. I wish to thank my teachers for demonstrating and sharing their experiences and insights regarding surgeries and patient care. I wish to thank Dr. Vernon N. Lee, Dr. Vinoo M. Cherian, Dr. Manasseh N., Dr. Kenny S. David, Dr. Venkatesh K., Dr. Rohit Amritanand, Dr. V.T.K. Titus, Dr. Pradeep M. Poonnoose, Dr. Anil T. Oomen, Dr. Vrisha Madhuri, Dr. Thomas Palocaren, Dr. Abhay, Dr. Alfred Job Daniel, Dr. Thilak Jepegnanam, Dr. P.R.J.V.C Boopalan for teaching and guiding me throughout my program.

I wish to thank my all my junior teachers Dr. Alfred Cyril Roy, Dr. Dan Barnabas, Dr. Sandeep Albert, Dr. Jeremy Bliss, Dr. Azeem Jabbar, Dr. VJ Chandy, Dr. Jerry George, Dr. Hariharan, Dr. Sumant Samuel, Dr. Abel Livingston, Dr. Kaushik Bhowmick, Dr. Jerry Nesaraj, Dr. Chandrasekhar, Dr. Rajamani for their guidance and imparting skills to operate and their willingness to teach me throughout.

I wish to express my gratitude to Dr. Vinu M. George and Dr. Vignesh Prasad for being beacons to look up to and strive to follow in their footsteps.

I wish to thank my colleagues for their constant help and support during my entire study and Post graduate program. I would like to personally thank Dr. Elvis Benjamin, Dr. Anil Chintada, Dr. Vinay T. Kuruvilla, Dr. Apurve, Dr. George Srampical, Dr.

Banteilang, Dr.Raunak Milton, Dr. Ajit Matthew, Dr. Chandan, Dr. Benjamin Matthew, Dr. Febin, Dr. Abhishek Jirel, Dr. Anto Anand, Dr. Joseph George, Dr. Rahul George, Dr. John Premnath, Dr. Reuben Cedric, Dr. Pandian, , Dr. Ramu, Dr. Jacob, Dr. Siddharth, Dr. Arun John Paul, Dr. Arunkumar, Dr. Roncy, Dr. Arun Gandhi, Dr. Jonath Samuel, Dr. Ashwin Sitaram and Dr. Samuel Santosh for the help and support and for making my time in CMC an enjoyable one.

I wish to express my sincere gratitude to Ms. Era Deepika Dayal for being a constant source of support and encouragement through everything and for her valuable help in all aspects of my PG dissertation.

I wish to thank Mr. Kasi for the help rendered in tracking down patients and aiding in data collection.

I wish to thank my family who has been my support system throughout and for being with me through everything.

# TABLE OF CONTENTS

# INTRODUCTION

Joint replacement surgeries have emerged as a procedure to enhance the lifestyle of a significant group of patients who have been affected by debilitating degenerative joint pathology. Arthroplasty provides a pain free, stable and mobile joint but a certain minority of patients might require revision surgery due to failure of the implant. The failure could be due to septic or aseptic causes.

Prosthetic Joint Infection (PJI) has emerged as a challenge to orthopaedic surgeons worldwide and it is a devastating complication. There has been a lot of recent research into diagnosis and treatment options. However, there have been not many studies to research the changing trends in organisms causing PJI and the resulting outcome of the same.

Our study was to mainly focus on this lacuna in the present knowledge regarding the organisms that cause PJI and to look at the outcome of patients who suffered from infections following arthroplasty.

We devised a study to prospectively follow up patients belonging to two retrospective cohorts and analyze the results to look at the outcome. There was historical evidence pointing towards *Staphylococcus aureus* and Coagulase Negative *Staphylococcus aureus* being the primary organisms implicated in PJI. We discovered that there was an increase in Gram Negative bacilli (GNB) causing PJI. We also noticed that there was a poor outcome in patients who have suffered PJI, especially when Gram Negative Bacilli were the causative organisms.

Extended spectrum β lactamase GNB in particular was seen to be on the rise in causing PJI and also had a very poor outcome with salvage procedures often required to completely eradicate the infection. This was an interesting observation and will require further research to fully understand the current spectrum of organisms that cause periprosthetic joint infection.

# AIM

To investigate the causes and outcome of infected arthroplasties.

# OBJECTIVES

1. To identify culture positive cases of arthroplasty infections.

2. To compare two cohorts to evaluate the changing trends of organisms causing infections from an initial time period (1.1.2007 – 31.12.2009) to the final time period (1.1.2012 – 31.12.2014).

3. To prospectively assess the outcome of patients with culture positive infected arthroplasties.

# LITERATURE REVIEW

Degenerative disorders of the hip and knee are increasingly common and there is an increase in joint replacement surgeries being performed for the same to alleviate symptoms and to restore a better quality of life.

The incidence of joint replacement surgeries has rapidly increased since Sir John Charnley pioneered the modern total hip arthroplasty. The prevalence of total hip and total knee arthroplasty surgery in the US in 2010 was estimated to be 0.83% and 1.52% respectively. (1) CDC estimated that in 2010 a total of 332,000 total hip and 719,000 total knee arthroplasty surgeries were performed in the US. (2)

There has been an increase in total hip and total knee arthroplasty surgeries done in India. Though the numbers might not be as high as in the US, there is a steady increase in the number of patients who have benefitted from adult reconstructive procedures of joints. The Indian Society of Hip and Knee Surgeons (ISHKS) established a registry in 2005 to collect and analyze data regarding causes, demography, and type of reconstructive procedures performed and also to look at the causes of failure of arthroplasty.

Prosthetic joint infections are a dreaded complication of total joint arthroplasty. The gravity of prosthetic joint infections is so severe that Sir John Charnley once considered stopping total joint arthroplasties altogether once he became aware of the complications of deep infections. However, he persevered by making the necessary changes to decrease the risk. (3) Prosthetic joint infection has garnered a lot of interest

in the past two decades and a significant research has gone into the same. Recent advances in understanding pathophysiology, etiology, diagnosis and management have led to an improvement in the understanding and outcome of infected arthroplasty.

# EPIDEMIOLOGY

## INCIDENCE

There has been a steady increase in the rate of Prosthetic joint infections as the number of index surgeries increase. Sir John Charnley initially reported the rates of infection in Total hip arthroplasty to be as high as 6.9% in 1969. (4) There has been a decrease in infection after introduction of measures to control infection in the operating room. A relatively new statistic by Kurtz et al revealed that the rates of infection after Total hip arthroplasty seemed to increase from 1.99% in 2001 to 2.18% in 2009 and the rates of infection after Total knee arthroplasty showed an increase from 2.05% to 2.18% in the same time period. (5) It is estimated that almost 65% of infections arise within the first one year after index surgery with the causative organism being successfully identified in 91% of the cases. (6)

The rates of infection after Total shoulder arthroplasty and Total Elbow arthroplasty have largely been from singe center studies. It is estimated that the rate of infection after a shoulder arthroplasty ranges from 0.8% to 0.9%, (7) and the rate of infection after an elbow arthroplasty is as high as 3.3%. (8)

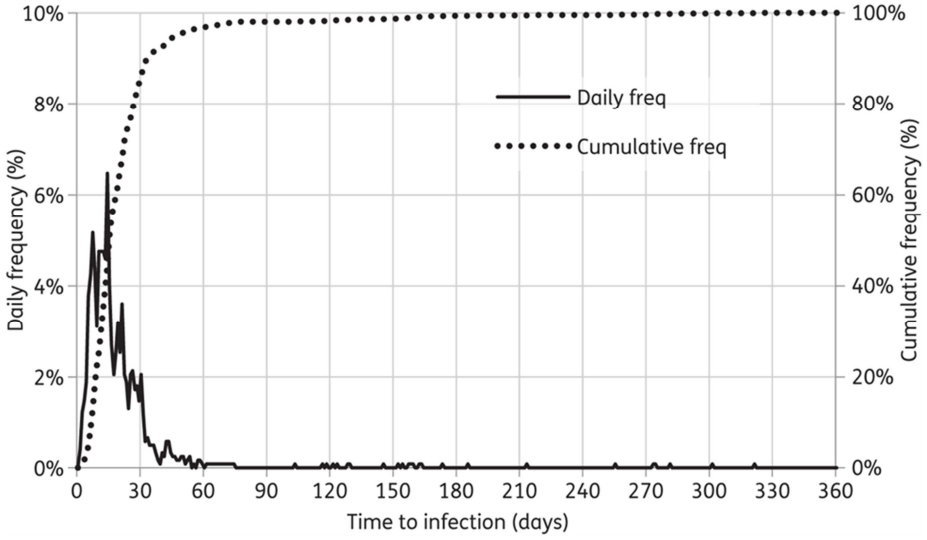



Fig.1 Showing onset of infection with respect to time from surgery (9)

## ECONOMIC BURDEN

Prosthetic joint infection (PJI) is a devastating complication that leads to significant burden to the patient in terms of health, hospital stay and financial strain. The cost of treatment of infected arthroplasty varies greatly, as there is no standard method of treatment. Though a two stage arthroplasty is increasingly becoming the accepted norm for treatment, there are a host of other methods to treat infected arthroplasty depending on the severity and scale of infection.

The economic burden of revision arthroplasty for infection has been widely studied in the US and UK among other countries. The Nationwide Inpatient Sample (NIS) database in the US estimated that the average cost of primary Total hip arthroplasty (THA) was $ 47,080 and the average cost of revision for infection was $ 70,753 in

2004. Similarly, the average cost of primary Total knee arthroplasty (TKA) was $ 35,320 and the average cost of revision for infected TKA was $ 63,705 in 2004. (10) The National Joint Registry in the UK estimated the average cost of aseptic revisions to be £11,897 and the difference in average cost between septic and aseptic revisions to be £10,040 in 2008. (11) These figures reveal that there is almost a two fold increase in the cost of a revision arthroplasty performed for PJI. These figures are excluding the cost of hospital stay, cost of antibiotics and the financial burden to the patient in terms of loss of pay.

## DEFINITION

The definition of Periprosthetic joint infection has been a subject of debate and there is no gold standard when it comes to defining the same. There have been several criteria that have been put forth for defining PJI. These criteria have undergone changes over time and are constantly being modified. The initial criteria placed more emphasis on culture and histopathology to diagnose PJI. These may be more sensitive and specific but there were false positive and negative results and also it was more cumbersome to obtain a histopathological sample. Hence, joint aspirate was introduced to look for serological markers. This too lacked specificity and in the meantime, joint aspirate to look for cell counts to diagnose PJI were introduced. The newer definition has inculcated all these modalities into the criteria for diagnosis of PJI.

## EVOLUTION OF CRITERIA FOR DEFINING PJI

1. Berbari et al in 1998 proposed the following criteria where one of the three being positive was considered PJI (12)
    - Two or more positive cultures grown on solid medium from intraoperative specimens grew the same organism
    - Sinus communicating with prosthesis or presence of purulence around the implant at the time of surgery
    - Acute inflammation consistent with infection on histopathological examination

2. Spangehl et al in 1999 proposed the following criteria where one of the two following criteria in bold or three of the five in italics being positive was considered PJI (13)
    - **Presence of open wound or communicating sinus**
    - **Presence of systemic infection with hip pain or purulent fluid in the joint**
    - *At least one positive culture grown on solid media during preoperative evaluation*
    - *At least 1/3 positive culture grown on solid media during intraoperative evaluation*
    - *Frozen section reveals more than 5 PMN cells/HPF*
    - *ESR more than 30 mm/hr*
    - *CRP more than 1 mg/L*

3. Parvizi et al in 2006 proposed the following criteria where three of the five being positive was considered PJI (14)
    - At least one positive culture on preoperative aspiration
    - At least one positive culture on intraoperative aspiration
    - Presence of purulence around the prosthesis during surgery
    - ESR more than 30 mm/hr
    - CRP more than 1 mg/L

4. Trampuz et al in 2007 proposed the following criteria where one of the three being positive was considered PJI (15)
    - Purulence around prosthesis during surgery for debridement or removal of prosthesis
    - Sinus tract communicating with prosthesis
    - Acute inflammation consistent with infection on histopathological examination

5. Schinsky et al in 2008 proposed the following criteria where two of the three being positive was considered PJI (16)
    - At least one positive culture growth on solid medium from intraoperative sample
    - Purulence around prosthesis during surgery for debridement or removal of prosthesis

- Acute inflammation consistent with infection on histopathological examination

6. Parvizi et al in 2008 compiled the following criteria where one of the two following criteria in bold or all three in italics being positive was considered PJI (17)
    - **One positive culture growth on solid medium from preoperative aspiration**
    - **Abscess or sinus tract communicating with prosthesis**
    - *Two or more positive intraoperative cultures or one positive growth on solid media*
    - *Abnormal histology*
    - *Presence of gross purulence in the joint*

7. AAOS in 2010 put forth new clinical practice guidelines with the following criteria for defining PJI (18)
    - High probability of infection:

      One or more symptom and at least one or more of the following
        - Risk factors
        - Warmth
        - Effusion
        - Redness
        - Communicating sinus tract

- Radiological evidence of loosening or osteolysis

- Low probability of infection:
  - No risk factors
  - Pain
  - Joint stiffness only
  - Physical examination findings
  - Radiological evidence of loosening or osteolysis

8. Infectious Diseases Society of America (IDSA) in 2012 put forth the following criteria for defining PJI (19)

   Definite:

   - Sinus tract communicating with prosthesis
   - Purulence around prosthesis in the absence of other factors

   Highly suggestive:

   - Acute inflammation consistent with infection on histopathological examination
   - More than 2 intraoperative cultures growing same organism or combined aspiration and culture
   - Culture growing a virulent organism from tissue or synovial fluid

9. The Musculoskeletal Infection Society in 2011 defined PJI as (20)

Major Criteria: (One of the two)

- Sinus tract communicating with the prosthesis
- Same organism isolated on two or more separate cultures from the affected joint

Minor Criteria: (Four out of six)

- Elevated Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP)
- Elevated synovial fluid WBC count
- Elevated synovial fluid neutrophil percentage (PMN %)
- Isolation of organism in one culture from affected joint
- Purulence of the joint
- More than 5 PMN/high power field (hpf) in 5 hpf during histopathological examination

10. The International consensus group met in 2014 and put forth a new and improved definition of PJI (21)

Major Criteria: (One of the two)

- Sinus tract communicating with the prosthesis
- Same organism isolated on two or more separate cultures from the affected joint

Minor Criteria: (Three out of five)

- Elevated Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP)
- Elevated synovial fluid WBC count or ++ on leucocyte esterase strip
- Elevated synovial fluid neutrophil percentage (PMN %)
- Single positive culture
- More than 5 PMN/high power field (hpf) in 5 hpf during histopathological examination.

11. The Centre for Disease Control (CDC) in 2015 further added quantifiable data to the above criteria and defined PJI as (22)

Major Criteria: (One of the two)

- Sinus tract communicating with the prosthesis
- Same organism isolated on two or more separate cultures from tissue or fluid from the affected joint

Minor Criteria: (Three out of five)

- Elevated Erythrocyte Sedimentation Rate (ESR) of more than 30 mm/hr and C-Reactive Protein (CRP) of more than 10 mg/L
- Elevated synovial fluid WBC count of more than 10000 cells/ µL or ++ on leucocyte esterase strip

- Elevated synovial fluid neutrophil percentage (90 %)
- Single positive culture
- More than 5 PMN/high power field (hpf) in 5 hpf during histopathological examination

Though there have been a multitude of criteria to define prosthetic joint infection, the criteria put forth by the International consensus group is the one that is most widely accepted and routinely followed.

## RISK FACTORS

Despite there being emphasis on perioperative methods to prevent PJI, there are a host of medical, environmental and habitual risk factors that can eventually predispose to infection in arthroplasties. The strategies to prevent the rate of PJI should ideally focus on the following risk factors. The risk factors can be broadly divided into preoperative risk factors, intraoperative risk factors and postoperative risk factors.

PREOPERATIVE RISK FACTORS

1. Malnutrition: There is a fivefold increase in the risk of wound complications when the total lymphocyte count is less than 1500 cells/$mm^3$ and a seven fold increase in wound complications when the serum albumin level is less than 3.5g/dL. Jaberi et al found that an absolute neutrophil count of less than 1500

cells/$mm^3$ and serum albumin level less than 3.5g/dL and serum transferrin level of less than 200 mg/dL predispose to infection. (23)

2. Anaemia: Preoperative anaemia predisposes the patient to receive allogenic blood transfusion which can increase the risk of postoperative wound infections. (24) Preoperative injections of Erythropoietin can be used to improve anaemia but it is a very expensive method of doing so and hence is not routinely followed. (25)
3. Obesity: The risk of infection rises from 0.36% in patients with normal BMI to 4.66% in morbidly obese patients. (26) The chance of wound dehiscence increases due to increase in surface tension at the surgical site. Obese patients suffer from 'paradoxical malnutrition' where they are malnourished despite their obesity. (27)
4. Uncontrolled Diabetes: Uncontrolled diabetes mellitus is defined as a random blood sugar level of > 200 mg/dL or a HbA1c value of > 7 gm%. The poor glycemic control leads to impaired wound healing and increases the risk of deep infections. (28)
5. Rheumatoid Arthritis: Patients with rheumatoid arthritis are likely to be on treatment with Disease Modifying Anti Rheumatoid Drugs (DMARDs) which have immunosuppressive properties. This immunosuppression leads to increased chance of wound dehiscence and thus increases chance of PJI. (29) Patients with Rheumatoid arthritis have a 1.8 to a 4 fold increase in rates of infection compared to patients without rheumatoid arthritis. (30)

6. Cardiac disorder: Congestive cardiac failure, valvular heart disease and pulmonary congestion increase the chance of infection. There is a high probability of patients with cardiac disorders consuming oral anticoagulants that lead to postoperative hematoma formation that could predispose to infection. (31)
7. Coagulopathy: Coagulopathy with an elevated International normalized ratio (INR) will lead to increased intraoperative bleeding and hematoma formation. (31)
8. Smoking: Smoking is a modifiable risk factor with potentially hazardous effects on tissue healing. Smoking causes decrease in tissue perfusion and impaired neutrophil activity which impairs humoral immunity. Nicotine also leads to vasoconstriction and hypoperfusion with increase in platelet aggregation and exaggerated thrombi formation further worsening blood supply. (32)
9. Chronic renal failure: Chronic renal failure patients on haemodialysis have a 22% risk of PJI when compared to 8% in patients who have undergone renal transplant. The cause for this may be multifactorial and hasn't been fully understood. (33)
10. Depression and alcohol abuse also increase the risk of infection after Total joint arthroplasty.

INTRAOPERATIVE RISK FACTORS

1. Skin Preparation: Skin preparation plays a vital role in reducing the bacterial load prior to incision. Hair should be removed from skin as close to the incision time as possible. (28) However, it is best to avoid mechanical methods like razor to prepare skin as it can lead to micro abrasions that would serve as a nidus for infection. Alcohol based preparation like Chlorhexidine has been found to be superior to Iodine for preparation of skin. (34)
2. Surgical gowns and gloves: There was no significant difference between using a surgical exhaust suit and standard occlusive gown. However, the gloves that were used for draping had an increased bacterial colony count. It has been recommended to change the outer glove after draping and also to change the outer glove prior to cementation or when the case is prolonged. (28)
3. Antibiotic impregnated cement: Jamsen et al reviewed the Finnish arthroplasty registry and found that there was a significant decrease in infections when antibiotic impregnated cement was used (0.68% vs 1.05%) (35)
4. Operating room configuration and traffic: Ritter et al reported a 97% reduction in bacterial contamination when laminar flow was used. (36) However, Salvati et al reported an increase in bacterial colonization in laminar flow settings. This was attributed to positioning of Operation room personal and the relation of wound to airflow. (37) Both agreed that reduced traffic in the operating room decreased the rate of PJI.
5. Surgery time: Prolonged surgery time increased the chance of infection. (38)

6. Wound closure: Proper wound closure with no wound gaping and judicious use of suture materials is absolutely essential in prevention of infection.

POST OPERATIVE RISK FACTORS

1. Indwelling catheters: Urinary catheters retained for more than 48 hours had an increased chance of urinary tract infection that could subsequently lead to PJI. (28)
2. Blood transfusion: Allogenic blood transfusion can increase the risk of postoperative wound infections. (24)
3. Wound drainage: Prolonged wound drainage can lead to an increase in deep infections. The risk of wound infection when there was prolonged drainage increased by 42% and 29% for THA and TKA respectively. (28)
4. Dental and Urological procedures: Hematogenous seeding of infection from a distant source is a dreaded complication in arthroplasty. All dental and urological procedures are to be covered by prophylactic antibiotics to prevent hematological seeding of infection. In 2012, the American Academy of Orthopaedic Surgeons and the American Dental Association put forth clinical guidelines where the role of prophylactic antibiotics was questioned. It was decided that prophylactic antibiotics would be administered based on individual requirement and maintenance of good oral hygiene would be promoted. (39)

# CLASSIFICATION

There are several useful classification systems that have been put forth to classify Periprosthetic Joint Infections. Fitzgerald et al were the earliest to classify the PJI into three types based on the time of infection and the course of deep infections.

FITZGERALD CLASSIFICATION (40)

Stage I Infection (Acute Fulminating Infections)

Acute fulminating infections present in the first three months after the index surgery, but most commonly in the first month. The most common cause is the presence of a hematoma that gets infected or the presence of superficial infections that track deeper.

Stage II Infection (Delayed Sepsis)

Delayed sepsis is a slow, indolent infection that developed in the first 26 months after the index surgery.

Stage III Infection (Late Hematogenous)

Late Infections arose in previously asymptomatic hips following arthroplasty. The mean time of incidence was between 23 to 51 months. It could be due to hematogenous seeding but could also be due to extremely indolent infection.

TSUKAYAMA CLASSIFICATION (41)

Tsukayama popularized this classification system in the 1990s and it was based on the timing of infection from surgery and on the mode of infection.
This system classified PJI into 4 categories.

Type I (Positive Intraoperative culture)

This includes patients who are undergoing revision surgery for presumed aseptic loosening and are incidentally found to have a positive culture. Some patients who fall into this category might not have a PJI.

Type II (Early Postoperative Infection)

This is similar to Stage I in the Fitzgerald classification where infection occurs in the first month after index surgery.

Type III (Late Chronic PJI)

This includes infections that occur after one month from the index surgery and includes delayed and late onset PJI from the Fitzgerald system.

Type IV (Acute Hematogenous Infection)

Acute hematogenous infection is used to describe infections that arise after a long period in a previously asymptomatic prosthetic joint. It denotes hematogenous seeding from a distant site that could be due to mucosal breach or infection elsewhere in the body.

McPHERSON STAGING SYSTEM FOR PJI (42,43)

The McPherson system classifies not only the type of infection but also the host. The system further classifies the local extremity where the prosthesis is placed. Thus, this system has three components and it allows for a more individualized treatment.

Infection Type

I – Early Postoperative infection (less than 4 postoperative weeks)

II – Hematogenous Infection (less than 4 week duration at any instant)

III – Late Chronic Infection (more than 4 week duration)

Systemic Host Grade

A – Uncompromised

B – Compromised (1-2 compromising factors)

C – Significant compromise (more than 2 compromising factors or one of the following)

- Absolute Neutrophil count less than 1000/$mm^3$
- CD4 T count less than 100/$mm^3$
- Intravenous drug abuse
- Chronic active infection at another site
- Dysplasia or neoplasm of the immune system

Local Extremity Grade

A – Uncompromised

B – Compromised (1-2 compromising factors)

C – Significant compromise (more than 2 compromising factors)

# PATHOGENESIS

## INITIATION OF INFECTION

Majority of PJI tend to occur in the first year after the index surgery. The earliest method by which infection reaches the prosthesis or periprosthetic tissue is through direct contact or via aerosols. (44) This occurs primarily at the time of surgery when the surgical field is exposed to the environment. A low inoculum of microorganisms is enough to initiate infection. Southwood et al showed that less than $10^2$ colony forming units (CFU) of *S.aureus* causes infection in the presence of prosthesis compared to $10^4$ CFU in regular tissue. (45)

Another mode of infection is contiguous spread from an adjacent site. (44) The microorganisms find an easy passage through disrupted tissue planes in the immediate postoperative period. Contiguous spread plays a major role in elbow PJI where there is minimal soft tissue and increased chance of wound breakdown.

The next method of infection is hematogenous spread from distant sites. Dental, endoscopic and urological procedures tend to breach the mucosa that could lead to bacteremia. Bacteremia in the presence of prosthesis can predispose to PJI.

## ADHERENCE OF BACTERIA TO IMPLANT

Adherence of bacteria to the implant is the first step in the initiation of infection (46). The implant with blood components adherent to it forms a 'conditioning film'. (47) The conditioning film enables bacteria to adhere on to an implant. There are two very distinctive methods of adherence: Reversible (nonspecific) and Irreversible (specific). (46) Reversible attachment is through nonspecific methods like physical and chemical properties of the bacteria. Biomaterials and the joint fluid also contribute to reversible adherence. Irreversible adherence on the other hand is mediated through specific receptors on the bacterial surface. (46)

## FORMATION OF BIOFILM

Biofilms are complex structures characterized by microorganisms that are embedded in an extracellular matrix. The community could be mono microbial or polymicrobial. The extracellular matrix is comprised of polysaccharides and proteins with interspersed nuclear material.

Gristina et al propounded an interesting statement 'the race for the surface' (48) that aptly describes the situation that prevails shortly following implantation of prosthesis. According to this concept, the adhesion of bacteria to the prosthesis and the integration of implanted biomaterials follow a very similar process.

There is a race between the host system to cover the prosthesis and the bacteria to adhere to the implant.

If the bacteria win the race, they display their survival tactic by the formation of a biofilm within which they can thrive. The bacteria secrete large amounts of extracellular slime to protect its cell wall. The glycocalyx and proteins in the biofilm stimulate monocytes to secrete $PGE_2$ that inhibits T lymphocyte action. (49)

Biofilm protects the bacteria from antimicrobial agents and from the host defence mechanism. (50) Thus, the treatment has to be directed towards elimination of the biofilm which is surgical intervention. However, there are certain drugs like Rifampicin may act against staphylococcal biofilms.

Though biofilms have been implicated in PJI, only recently have viable bacteria been isolated ex vivo from explanted prostheses. (51)

Jeff G. Leid et al studied the properties of maturing and fully mature staphylococcal biofilms under static and laminar shear conditions and found that human leucocytes do have the ability to bind to the maturing biofilms under static conditions and to fully mature biofilms under laminar stress conditions. In biofilms that were grown in vitro under laminar stress conditions, the leucocytes exhibited an ability to bind and phagocytose planktonic bacteria but not the ones inside the biofilm. (52)

Another adverse implication of biofilm in PJI is that it reduces sensitivity of cultures for diagnosis as it is adherent to the surface of the prosthesis. Hence, sonication of implant may be necessary for diagnosis of the organism.

## PROPAGATION OF INFECTION

Animal model studies have revealed that once the inoculum infects the joint space like in Fitzgerald stage I infections, it is initially confined to the joint space where histology reveals granulomas with large neutrophils. The infection then slowly spreads to the proximal 1/3 of the metaphysis over the next 3 weeks. If the infection is left untreated it creeps to involve the remaining metaphysis and in some cases the diaphysis also gets infected. (53) If there is hematogenous seeding like in Fitzgerald stage III infections, the metaphysis gets infected first due to the rich vascular supply of the metaphysis. (54)

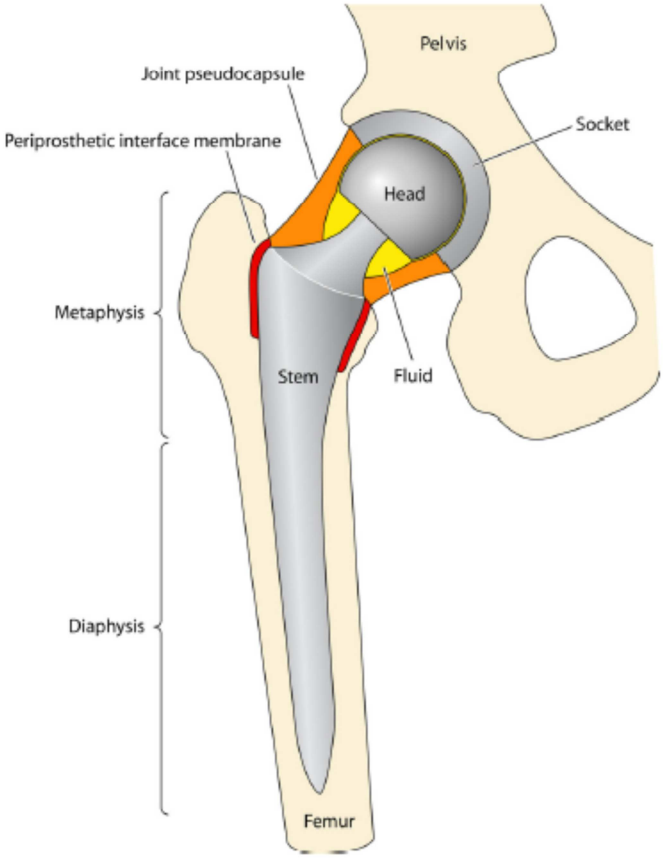



Fig. 2 Schematic showing a THA in place with relevant structures highlighted (44)

## MICROBIOLOGY

The spectrum of organisms that cause PJI is wide and varied. It is important to have knowledge of the microorganisms commonly implicated in PJI to form a protocol for administration of perioperative antibiotics. National surveillance data for England in 2011 estimated that most of the PJI were caused by *Staphylococcus aureus*. The data indicated that *Staphylococcus aureus* was responsible for infection in 44% cases with 20% being resistant to methicillin.

Coagulase-negative staphylococci also featured prominently (31%), with the remaining infections split between *Enterococci* (12%) and *Escherichia coli*, *Enterobacter spp.*, *Pseudomonas spp.*, and *Streptococci* (7% each). Overall incidence of polymicrobial infections was 28%. (9) Though staphylococcus is the most common cause of PJI, there is an increase in the incidence of gram negative bacteria over the past few years. (55) There is also an increase in the incidence of Culture negative PJI due to administration of antibiotics prior to culture. Fungal PJI have also been reported.

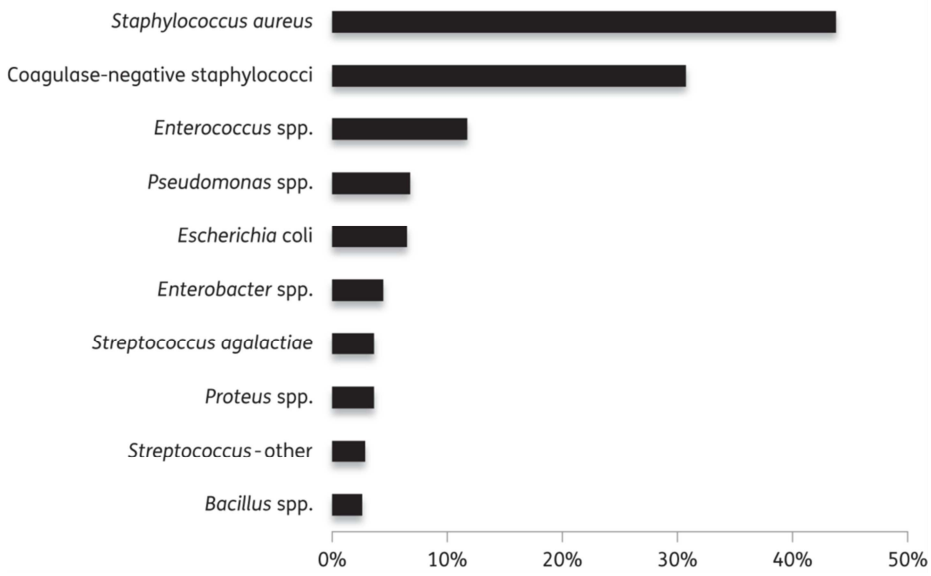



Fig. 3 Showing distribution of organisms (9)

## CAUSATIVE MICROORGANISMS

### *Staphylococcus aureus*

It is a very important pathogen in relation to PJI. Several studies have reported *S.aureus* to be the most common pathogen to cause prosthesis related infection. It has attained this notoriety due to its virulence and frequency. *S.aureus* is important not only as a leading cause of infection after arthroplasty but also due to the fact that it causes serious invasive infections and causes nosocomial infections that could again lead to PJI. (56)

*S.aureus* is the most commonly identified pathogen in cases which were treated with debridement, antibiotics and implant retention (DAIR). (41,57) The advent of Methicillin resistance in recent times has further complicated the treatment of *S.aureus* due to the limited range of antibiotics available for treatment. (58)

### Small colony variants (59)

Small colony variants are a subtype of *S.aureus* that cause persistent and recurrent infection. They vary from S.aureus due to a slow rate of growth and decreased pigmentation and hemolysis. Small colony variants (SCV) are difficult to treat due to resistance to aminoglycosides and cell wall active antibiotics. They have an ability to persist in the intracellular environment and possess the ability to revert to a highly virulent and rapidly dividing form making treatment difficult. (59)

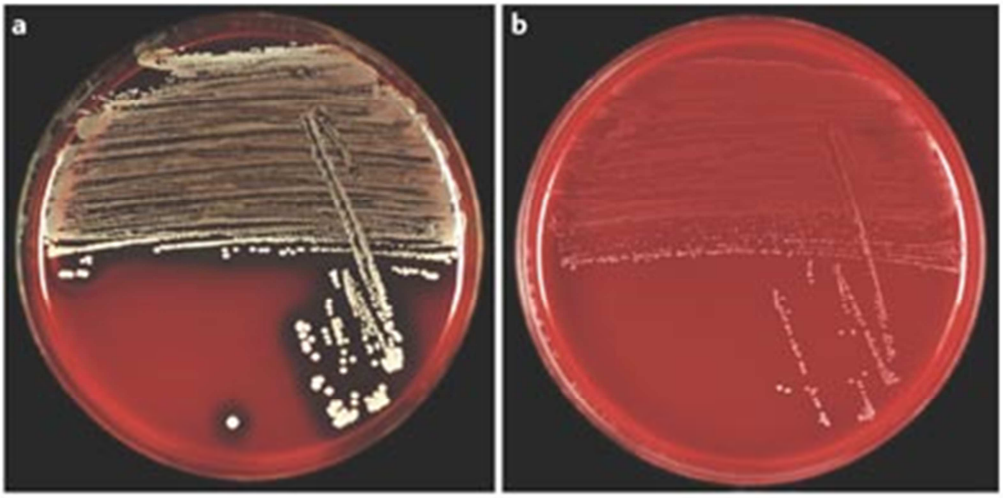



Fig. 4 a- Normal colony b- SCV on Columbia agar (60)

*Coagulase negative Staphylococcus species*

A number of species together constitute what is known as coagulase negative staphylococcus (CONS). CONS are frequently found as commensals on the surface of skin and can be considered as opportunistic pathogens. *Staphylococcus epidermidis* is the most common of the organisms in this group. *Staphylococcus epidermidis* shows affinity for prosthesis and adheres to the surface of the implant and readily produces biofilm. (61,62) Other species that cause PJI are *Staphylococcus simulans* (63), *Staphylococcus caprae* (64), and *Staphylococcus lugdunensis*. (65) Oxacillin resistance is commonly seen in CONS causing PJI with the exception of *Staphylococcus lugdunensis*. (66)

*Streptococcus species*

Streptococci cause a variety of infections in humans but however are implicated in less than 10% of PJI. A number of β hemolytic streptococci cause PJI, especially the ones belonging to Lancefield group A(67) , B (68), C (69) and G (67). *Streptococcus gallolyticus* subsp. *gallolyticus* (formerly *Streptococcus bovis* biotype I) has been known to cause PJI. (70) *Streptococcus viridans* is an uncommon cause of PJI (67) and *Streptococcus pneumoniae* has also been known to cause PJI. (71)

Group B and G streptococci are the most common streptococci to cause arthroplasty infections. (67) Group B streptococci frequently cause delayed or late onset PJI and most of those patients have at least one co morbid illness. (72) The infection is predominantly due to hematogenous seeding from either genitourinary, gastrointestinal tract or skin. (68)

*Enterococcus species*

Enterococci are rare causes of PJI and are predominantly seen in early onset PJI as a part of polymicrobial infection. (73) The source of infection is thought to be hematogenous seeding from the genitourinary or gastrointestinal tract.

Aerobic gram negative bacilli

Aerobic gram negative bacilli are similar to enterococci in causing infection by leading to early onset PJI. (73) Gram negative bacilli are seen as a part of monomicrobial infection due to hematogenous seeding or as a part of

polymicrobial infection. The most common pathogen in the aerobic gram negative bacilli group is *Escherichia coli* which affects the hip more than the knee due to its proximity to the gastrointestinal tract. (74) *Pseudomonas aeruginosa* is the next most commonly reported pathogen. (75) These group of organisms cause early postoperative infections due to its high virulence. They affect the older age group more commonly than the younger age group which is predominantly infected by gram positive bacteria. (75)

*Propionibacterium acnes*

*Propionibacterium acnes* is a low virulence, slow growing, anaerobic gram positive bacilli that is found in the skin and sebaceous glands and is inoculated onto the prosthesis at the time of surgery. (44) It is commonly associated with Prosthetic shoulder infections. (76,77) Patients who suffer from *P.acnes* PJI will have normal levels of ESR and CRP even when the organism is proved by microbiological methods. (78)

The infections caused by *P.acnes* have an indolent course and do not cause much symptomatic discomfort to the patients.

Other anaerobic bacteria

The other anaerobic bacteria that have been implicated in PJI are *Clostridium species, Bacteroides fragilis, Peptostreptococcus species* and *Actinomyces species.* (44) These organisms frequently are a part of polymicrobial infections and have been reported in 12% of polymicrobial infections. (79) *Clostridium*

*species* are frequently reported to cause PJI in patients who are suffering from some disease of the gastrointestinal tract. (44) *Peptostreptococcus species* infections are common in patients who undergo dental procedures. (80) Intravenous drug abusers could get their prosthesis infected by *Actinomyces israelii.* (81)

These anaerobic bacteria predominantly cause late onset PJI and could infect the prosthesis via hematogenous seeding.

Polymicrobial Infection

Polymicrobial infection occurs more during the early postoperative period. Cobo et al showed that 35% of polymicrobial PJI occurred in the first three months after index surgery compared to less than 20% during other time frames. (73) *Enterococcus species, Staphylococcus aureus* and aerobic gram negative bacilli most commonly *Pseudomonas aeruginosa* are the most commonly identified organisms in a polymicrobial infection, each being present in more than 25% infections. (79)

Polymicrobial infections are associated with rheumatoid arthritis, (82) higher co morbidity index, (83) age more than 65 and wound drainage and dehiscence after surgery. (79)

Other bacteria

The following bacteria have been reported in literature in the form of case reports to have caused PJI. Several *Corynebacterium species* have been implicated in PJI particularly prosthetic shoulder infection (84) with *Corynebacterium jeikeium* causing infection that is resistant to a wide range of antibiotics. (85) *Listeria monocytogenes* PJI was typically associated with meningoencephalitis in older individuals and in immunocompromised patients. (86) Zoonotic organisms like *Brucella species* (87) and *Pasteurella multocida* (88) have also been showed to cause PJI. Infection with *Pasteurella multocida* is seen after scratch, lick or bite from a cat or a dog. (88) *Coxiella burnetii* has also been reported to cause PJI. (89)

Mycobacterium species

*Mycobacterium tuberculosis* complex is an uncommon cause of PJI accounting for only 0.3% of infections in developed countries. (90) However, in patients who had a previous history of septic arthritis of the joint due to *Mycobacterium tuberculosis* complex, the chance of Mycobacterial PJI is as high as 31%.(44) PJI due to *Mycobacterium tuberculosis* complex can also occur in patients with no active or latent history of infection with *Mycobacterium tuberculosis* complex.(91) It typically affects the hip and knee but the hip is involved more often. (90) Non tuberculous mycobacteria very rarely cause PJI. One single institute study spanning 38 years reported 8 cases infected by rapidly growing

mycobacteria. (92) PJI due to *Mycobacterium avium intercellularae* has been reported in immunocompromised patients with HIV/AIDS. (93)

Fungal Infection

Fungi cause less than 1% of PJI. (94) *Candida species* is found in majority of the cases with *Candida albicans* causing 80% of the infections (95) However, *Candida parapsilosis* was the most common species identified in a single large center study in Southeast Asia. (94) *Aspergillus species*, (96) Dimorphic fungi, (97) Pigmented yeast, (96) Dematiaceous fungi, (96) and filamentous fungi (98) have also been reported in literature to cause fungal PJI.

Majority of fungal PJI occurred after revision arthroplasty. (96,99) Prior bacterial PJI, preceding antimicrobial use, immunosuppressive therapy and diabetes are risk factors for fungal PJI. (99) *Aspergillus* species has been shown to cause infections in immunocompetent individuals in several cases, unlike pulmonary infections due to *Aspergillus spp.*, which occur in immunocompromised individuals. (100)

Culture negative PJI

Culture negative PJI is defined as presence of purulence around prosthesis during surgery, acute inflammation suggestive of infection on histopathology or sinus tract communicating with the prosthesis but failure to grow any organism on microbiology culture samples.(44,101)

Culture negative PJI can occur due to prior use of antibiotics, inadequate use of microbiological methods or inability to diagnose the organism with existing microbiological tools. (89,101–103)

The incidence of Culture negative PJI is around 5-35% (104) and it presents as a late onset type. (104)

Withholding antibiotics prior to obtaining culture and improving sensitivity of microbiological tools could help bring down the rates of culture negative PJI.

## DIAGNOSIS

Diagnosis of PJI with accuracy and efficiency is truly a unique challenge. (203) Despite there being a multitude of tests to aid in the diagnosis, one cannot stress the fact that history and physical examination are of paramount importance. As a general rule any patient with a prosthetic joint in place, who presents with pain in that particular joint, should be considered to have PJI unless proved otherwise. (105) The approach to diagnosis is twofold: The first is to prove that PJI exists and the second is to isolate the organism and determine the antimicrobial sensitivity.(44)

For years, there was inadequate research regarding the diagnosis of PJI due to the lack of a definitive diagnostic criterion. Over the past decade there has been a refinement in criteria for diagnosis of PJI.

Bacteriological diagnosis of PJI is essential. The low sensitivity of periprosthetic tissue in diagnosis could be attributed to the fact that most of the organisms are organized into biofilms and are sessile on the surface of the implant with few free planktonic forms that can be readily identified.(50)

## PERIPHERAL BLOOD TESTS

Peripheral blood tests rely on the host response to the infecting pathogen.

### Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP)

ESR and CRP are the most frequently used markers and have been included in almost all the newer diagnostic criteria. These tests are relatively inexpensive and are widely available. Berbari et al in a metaanalysis found the combined sensitivity and specificity to be 88% and 74%.(106) Tande et al reported that when the levels of ESR was considered to be 30 mm/hr and when CRP was more than 10 mg/L then the sensitivity and specificity was 96% and 56% respectively.(44)

The levels of ESR and CRP increase soon after an arthroplasty with CRP reaching its peak value earlier than ESR. (107,108) In the absence of infection, the level of CRP normalises after 3 weeks and ESR takes 6 weeks to normalise.(108) These values may take longer to normalise after knee arthroplasty than after hip arthroplasty.(107)

Elevation in ESR and CRP levels after 3 months may suggest infection (109) but this has to be correlated clinically. ESR and CRP could also be elevated in

patients who develop heterotopic ossification and are unreliable in patients with inflammatory arthritis.(110)

*Coagulase negative staphylococcus, Candida, Corynebacteria, Mycobacteria, Actinomyces* and *Propionibacter acnes* can produce PJI without elevation of ESR and CRP.(111)

Interleukin 6 (IL-6)

It is produced by macrophages and monocytes and is a newer and promising modality in the diagnosis of PJI. It holds a theoretical advantage over ESR and CRP in returning to normal shortly after arthroplasty. IL-6 levels peak the same day with a mean half-life of 15 hours.(112) Berbari et al in a metaanalysis compiled data from three studies and reported a sensitivity and specificity of 97% and 91% respectively. (106) IL-6 was found to be consistently elevated with a value more than 10 pg/L in patients with PJI.(113) Due to the lack of robust clinical data and the fact that IL-6 is not readily available everywhere, IL-6 is not a part of the regular investigations for PJI.

Procalcitonin

Serum procalcitonin has been routinely used in diagnosing a variety of infectious conditions. The use of procalcitonin for PJI was studied by Bottner et al and they found that the sensitivity and specificity was 33% and 98%

respectively.(114) It is more readily available than IL-6 but further data is needed before this can be recommended for diagnosis of PJI.

## SYNOVIAL FLUID ANALYSIS

Synovial fluid for analysis can be obtained preoperatively and postoperatively. Obtaining synovial fluid from the knee joint is easier and can be performed as an office procedure whereas obtaining synovial fluid from the hip joint might require fluoroscopic guidance. Synovial fluid is analyzed for nucleated cell counts, percentage of neutrophils, leucocyte esterase strip and bacterial culture.(44)

### Nucleated cell count and Differential neutrophil count

There have been multiple studies that have looked into the synovial fluid white cell count for diagnosis of PJI. Though there is no definitive consensus, studies by Ghanem et al (115) reported more than 1100 cells/μL was predictive of infection for Total knee arthroplasty and Schinsky et al (116) suggested than more than 3000 cells/μL was suggestive of infection post Total hip arthroplasty.

Numerous studies have looked at the percentage of neutrophils for defining PJI and there are reports' varying from 65% to 95%, however, more than 90% seems to have the most sensitivity and specificity.

The synovial fluid that has been obtained for analysis has a good chance of being contaminated with blood and thus Ghanem et al proposed the following formula for calculating the estimated WBC percentage:

$$WBC_{adjusted} = WBC_{observed} - [(WBC_{blood} \times RBC_{fluid} / RBC_{blood})]_{predicted}$$ (117)

Leucocyte Esterase

Leucocyte esterase is an enzyme that is secreted by activated neutrophils that have migrated to the site of infection. The leucocyte esterase strip has been in use for decades to diagnose urinary tract infection. Parvizi et al recommended the use of leucocyte esterase strip for PJI. (118)

The leucocyte esterase strip is a colorimetric method that has 4 reactions: no colour change, trace, + or ++. It has a sensitivity of 80.6% and specificity of 100% when used for PJI.(118)

The advantage of using this test is that it is inexpensive and requires only one drop of synovial fluid and takes less than one minute for diagnosis. The main disadvantage is that it is a colorimetric test and blood contamination can alter the results.(119)

Gram Stain

Hans Christian Gram in 1884 described Gram staining of bacteria based on the biochemical differences in the cell wall of different bacteria.(120) Morgan et al studied the use of gram stain on intraoperative samples for PJI and found that it

had a very low sensitivity (27%) though it was very specific.(121) Hence, he recommended against use of gram stain as a diagnostic tool in PJI.

α defensin

Defensins are antimicrobial peptides that are a part of the innate immune system that do not require prior sensitization to act.(122) α defensins are expressed by PMN cells(123) and by monocytes and lymphocytes.(124)

Deirmengian et al showed that α defensins outperform the leucocyte esterase strip (125) and have a sensitivity of 99% in combination with CRP.(125)

α defensin estimation is a newer modality of diagnosis and requires validation with more studies.(126)

Other synovial fluid biomarkers

Cytokines like IL-1, IL-8, IL-17,(127) IFN-δ (128) and biomarker TNF α (129) are found to be elevated in the synovial fluid in PJI. These are newer modalities and need further studies regarding their sensitivity and specificity and feasibility in use for PJI.

Synovial fluid culture

Culture of periprosthetic fluid and tissue is very important for diagnosis. One single culture being positive has a low sensitivity due to potential chance of contamination. Trampuz et al showed that two intraoperative samples growing

the same organism was sufficient for diagnosis(15) and this has been incorporated into the consensus criteria for diagnosing PJI.(21)

A single positive culture of a low virulent organism can be considered contamination whereas a single positive culture with a virulent organism has a strong predictive value for PJI.

The specific media used for culture of periprosthetic tissue has not been studied extensively. Majority of studies used aerobic and anaerobic blood agar and some used thioglycolate broth.(130) Hughes et al showed that using four different media was gold standard for detecting infection in periprosthetic tissue.(131)

Traditionally aerobic cultures are observed for 4 days and anaerobic for 7 days as the identifying contaminants increases. This may be insufficient in conditions like Prosthetic shoulder infection with organisms like *P.acnes* that take longer to incubate. Butler et al suggested that both aerobic and anaerobic cultures be observed for 14 days to identify organisms that might longer to incubate.(132)

## RADIOLOGICAL MODALITIES

Imaging has a supportive role in diagnosis of PJI but not a definitive role.

### Plain Radiograph

Plain radiograph is the most commonly used modality for identifying septic or aseptic osteolysis. Plain radiographs can reveal periprosthetic osteolysis, loose

components, soft tissue gas, effusion or periosteal new bone formation that could suggest infection.(133)

It is not possible to differentiate between septic and aseptic loosening based on a single radiograph alone and will require radiographs done after a certain time interval.(134) The loosening in aseptic loosening progresses slowly whereas there is rapid progression of loosening with destruction of bone in septic loosening.(133)

Advanced Imaging Studies

Computed tomography may help to distinguish septic from aseptic loosening. Presence of periosteal new bone formation and presence of a soft tissue shadow adjacent to areas of osteolysis could suggest infection. (135,136)

Ultrasonography can be used to identify periprosthetic soft tissue collection. (136)

MRI can be used for identification but it has a very limited use due to the appearance of artifacts. Though there are methods to minimize artifacts(137) they are not able to enable adequate visualization around the prosthesis.(138)

Nuclear Imaging

Three phase bone scintigraphy is a widely used imaging technique for diagnosing PJI. A radioactive isotope is attached to a compound that collects in

bone and will emit gamma rays from areas of high metabolic activity which can be picked by gamma cameras. The intensity of uptake is measured at three time points with respect to blood flow: Immediate, blood pool for 15 minutes and a delayed scan at 2-4 hours.(139) Uptake at blood pool and late phase suggest PJI. However, this test lacks specificity.

Radioactive $^{111}$In can be used to label autologous leucocytes, which are injected and the uptake with a three phase scan is obtained at 24 hours in an effort to increase specificity. The scan is considered positive when there is uptake on the labeled leucocyte image but no uptake on a late image in the three phase scan.(140)

Positron Emission tomography with $^{18}$F fluorodeoxyglucose (FDG-PET) has been found useful in diagnosing PJI. It has a sensitivity of 82.1% and a specificity of 86.6%.(141) The only prohibitive factor is the high cost involved.

HISTOPATHOLOGY

Histopathology that reveals acute inflammation with neutrophilic infiltration either on a frozen section or a well fixed sample strongly suggests a PJI. The advantage of this method of evaluation is that it is not affected by perioperative antibiotics and if a frozen section is used, the reports are available for the surgeon on table. (44) However, some organisms like *P.acnes*(142) and Coagulase negative staphylococci(143) do not show a robust neutrophilic response.

The presence of 5 PMN in a high power field in 5 high power fields is the followed norm for diagnosis of PJI which has been included in the consensus for diagnosing PJI.(21,144)

The commonest areas for obtaining tissue for histopathology are joint pseudocapsule and the periprosthetic interface membrane. The sensitivity of samples from periprosthetic interface membrane was 83% compared to 43% from the pseudocapsule.(145)

Morawietz et al classified the periprosthetic membrane into four types: (146)

Type I or 'wear particle induced' which contains macrophages with polyethylene and metal wear particles and multinucleated giant cells.

Type II or 'infectious type' which has low grade and high grade forms. The low grade shows chronic granulation and the high grade shows neutrophilic infiltration.

Type III or 'combined type' has features of type I and II.

Type IV or 'indeterminate type' has less cells and more connective tissue.

## SONICATION OF EXPLANTED PROSTHESIS

There has been a considerable interest of late to dislodge bacteria found on the surface of implants and to culture them. It is easy to culture smaller prostheses like intravenous catheters but it is difficult to culture larger prosthesis.

Sonication was first realized by Tunney et al in the 1990s and it has undergone considerable refinement after that.(147) Sonication has now emerged as a practical and very effective way to dislodge bacteria from the surface of the

prosthesis. The explanted prosthesis is placed in a container with 400 ml ringer lactate (15) and is placed on a tabletop vortex for 30 seconds. Following this, low frequency ultrasound waves are passed through the fluid creating areas of high pressure and areas of low pressure. Microscopic bubbles form during the low pressure phase and collapse during the high pressure phase, dislodging bacteria from the surface of the prosthesis in the process.(148) Esteban et al introduced centrifugation of the sonicated fluid to further increase the yield.(149)

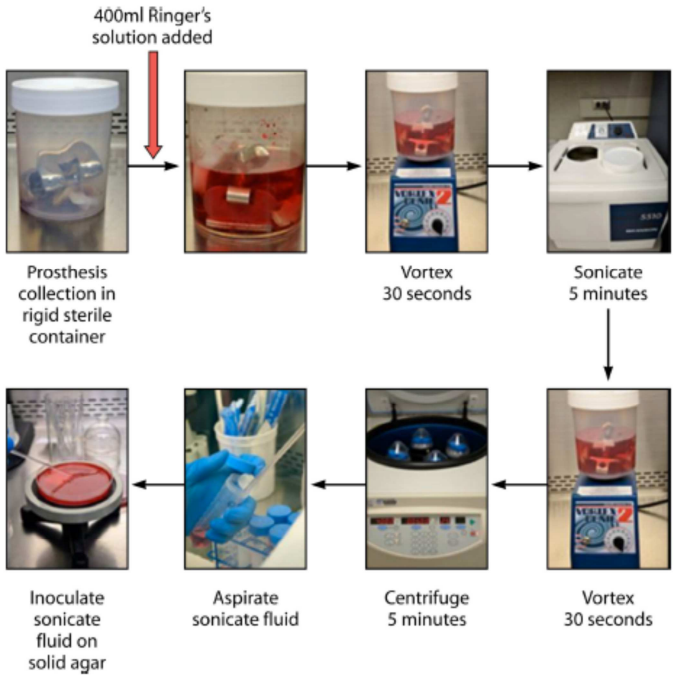



Fig.5 Sonication of explanted prosthesis

Several studies have reported a better sensitivity for sonicated fluid (62-94%) compared to periprosthetic tissue (54-88%). (149,150) Vortexing alone could

be a viable alternative to sonication in dislodging bacteria in labs which don't have facilities for sonication.(151)

MOLECULAR METHODS

Advances in medicine have led to various sophisticated methods to be used in diagnosis of various diseases. One such application is the use of molecular methods like PCR for diagnosis of PJI. PCR has an advantage over conventional methods in being quicker and having higher sensitivity when compared to conventional methods of diagnosing infections, particularly in patients who have taken a course of antimicrobial drugs.

Polymerase Chain Reaction (PCR)

PCR relies on the use of forward and reverse primers to match specific sequences in target nuclear material. The most common identification gene for bacteria is the 16s rRNA gene that is found in almost all bacteria. Identification of the 16s rRNA is called the 'broad base approach'. The advantage of using PCR for diagnosis is that it doesn't need viable bacteria to diagnose infection. Nuclear material from viable and necrotic areas that may contain bacterial DNA and RNA are sufficient for diagnosis. Bergin et al reported a sensitivity of 91% and a specificity of 100% with the use of PCR.(152)

The use of PCR for diagnosis does have its disadvantages. One of the reagents used in PCR called Taq polymerase is produced by a recombinant method from *Escherichia coli* and hence that increases the rate of false positive results. The

broad base approach also detects trace contamination with clinically irrelevant organisms.

Matrix Assisted Laser Desorption/ Ionisation time-of-flight mass spectrography

MALDI-TOF MS is a technique that causes soft ionization of intact bacteria and the bacterial extract. It determines the molecular structure of the organism by analyzing the difference in mass between the ions in the mass spectrum.(153)

The advantage is the ability to identify organisms with just a fraction of the sample and also to identify genes that lead to antimicrobial resistance.(154,155) The prohibitive factors are the cost and availability.

Ibis T5000 Biosensor

The Ibis T5000 combines broad base PCR and mass spectrography and is more accurate than conventional PCR.(156) However, similar problems of high false positives exist.

NOVEL DEVELOPMENTS AND FUTURE PROSPECTS(157)

The Shirtliff research group and the Smeltzer research group are currently involved in looking at the following methods for diagnosis and treatment of microorganisms and biofilms:

- Detection of anti-biofilm antibodies via ELISA and Lateral flow Immunoassay

- Biofilm diagnosis and localization by labeled anti-biofilm antibodies
- Photoacoustic diagnosis and photothermal infection elimination by antibody directed nanoparticles

## TREATMENT

The treatment for PJI involves both medical and surgical methods and requires multiple departments to work together to achieve a good outcome.

Treatment success is defined as clinical and microbiological eradication of the infection without any relapse and freedom from any subsequent surgical intervention for the same organism and freedom from mortality related to PJI. (158)

Temporal classification of success: (158)

- Short term – 2 years
- Midterm – 5-10 years
- Long term – more than 10 years

Treatment failure was considered when there was need for revision surgery for any reason,(159) requirement of additional or suppressive antibiotics beyond the initial treatment course,(160) nonfunctional arthroplasty(161) or death.

Cobo et al reported a mortality of 3-4% in patients suffering from PJI who were treated with debridement and implant retention.(73) Raut et al reported a metaanalysis that showed no mortality after treatment for PJI with exchange arthroplasty.(162)

The various treatment options available for PJI are open or arthroscopic debridement with implant retention, resection arthroplasty, One stage or direct arthroplasty exchange, Two stage exchange arthroplasty, Arthrodesis, Amputation or long term antibiotic suppression without surgery. The goal of treatment is to remove all infected tissue and hardware or decrease biofilm burden if the prosthesis is retained.(44)

## DEBRIDEMENT, ANTIBIOTICS AND IMPLANT RETENTION (DAIR)

The DAIR procedure should be performed using an open arthrotomy and the joint is thoroughly irrigated first and debrided with removal of necrotic tissue, any retained hematoma and purulence around the prosthesis. The stability of the prosthesis is checked intraoperatively and any loose components are exchanged. The joint space is then aggressively debrided and irrigated and closed over a suction drain. This procedure can also be performed arthroscopically but the debridement would be limited and the chance of failure increases fourfold.(163)

Antibiotics are withheld till culture is obtained and then broad spectrum antibiotics are started that are changed over to specific antibiotics after

availability of culture.(163–165) The recent IDSA recommendation is to give 4-6 weeks of intravenous antibiotics for organisms other than *Staphylococcus* or when Rifampicin combination therapy can't be used.(166) Most clinicians prefer to use suppressive oral antibiotics for a variable time period as the implant is retained. However, the chance of failure is highest in the first 4 months following stoppage of antimicrobial agents.(163) Leone et al suggested that antibiotics can be stopped once CRP levels return to normal and when there are negative nuclear imaging results.(167) As the chance of false positive with nuclear imaging scans are high, there is still no definitive consensus on stoppage of suppressive antibiotics.

DAIR should be used only in patients with a short duration of symptoms, stable implant and no sinus tract.(166,167) The pathogen should be susceptible to antimicrobial agents.(168) DAIR can be used in early postoperative infections (less than 1 month from index surgery) or in acute hematogenous infections (duration less than 3 weeks) and has a good success rate if performed immediately after onset of infection.(164)

The presence of a sinus tract(164,168) and infection due to *Staphylococcus aureus* has a high chance of failure when DAIR is practiced.(163–165) Methicillin resistant *Staphylococcus aureus,*(169) Vancomycin resistant *Enterococci*,(169) and fluoroquinolone resistant gram negative bacilli(170) also have high rates of treatment failure. Patients who develop failure with DAIR ultimately undergo a two stage revision arthroplasty.(171)

## SINGLE STAGE OR DIRECT EXCHANGE ARTHROPLASTY

One stage exchange arthroplasty is a less frequently performed procedure. Here, an open arthrotomy is done and debridement with removal of prosthesis and PMMA (Polymethyl methacrylate) is performed. Aggressive debridement and irrigation is performed following that with reimplantation of a new prosthesis with antibiotic impregnated PMMA cement.(44)

Several antimicrobial protocols are followed but the most commonly followed protocol is 4-6 weeks of intravenous antibiotics followed by oral antibiotics for 3-12 months.(172,173) Others recommend short course of intravenous antibiotics during the immediate postoperative period and oral antibiotics for 6 weeks to 6 months.(173,174)

One stage exchange arthroplasty is frequently performed for the hip and there have been very reports of direct exchange arthroplasty being used for the knee. Patients who undergo one stage exchange need to have a good bone stock, susceptibility of the organism to oral antibiotics and good surrounding soft tissue condition.(166,167) Patients with a draining sinus are typically treated by two stage exchange arthroplasty.(166,167)

Several studies have reported a success rate of around 84-100% (172,174)

## TWO STAGE EXCHANGE ARTHROPLASTY

A two stage exchange arthroplasty also known as staged exchange is widely considered to be the most definitive surgery in terms of eradication of infection and preservation of joint function. It involves at least two surgeries. In the first, the cultures are obtained and debridement is performed with removal of the prosthesis and cement. An antibiotic impregnated spacer is placed. Pathogen specific antibiotics are given for 4-6 weeks followed by 2-6 weeks of antibiotic free period (159) during which the patient is evaluated for signs of infection. If there is persistent infection, redebridement is performed with further antibiotic therapy. When the infection settles the second stage surgery is performed. During the second stage, tissue is taken for frozen section evaluation and a new implant is placed with antibiotic impregnated PMMA if the frozen section doesn't show features of active infection. Intravenous antibiotics are given till the culture reports from reimplantation surgery are ready and if there is any evidence of infection antibiotics are continued for a variable period of time.(44)

The antibiotic loaded spacers are of two types: Static and articulating. The static spacers are fashioned by hand and are placed to fill the void in the joint. Articulating spacers can be used to preserve the joint space and provide a reasonable range of movement. Articulating spacers can be either commercially preformed or made with custom moulds. It can be either made of PMMA or a

composite of PMMA, metal and polyethylene.(175) Niraj et al suggested the use of resterilised prosthesis as a temporary spacer(176) but it's not widely accepted. (177)

Antibiotic loaded articulating spacer serves two functions:

- Preserves joint position, prevents joint contractures and enhances comfort between the first and second stages.
- Local antibiotic elution between the first and second stage.

The antibiotic has to be heat stable and water soluble to enable elution into the surrounding tissue.(175) Two or more antibiotics may be used in a single spacer to provide broad spectrum coverage. An aminoglycoside is often used with Vancomycin in the spacer.(178) Typically 1-3 g of Vancomycin is mixed with 1.2-4.8g of Gentamicin or Tobramycin and is added to 40g of cement.(178,179) Spacers should use a high dose of antibiotics (more than 3.6g/40g) compared to less than 1g/40g cement used for fixation of prosthesis.(180)

As there is no implant that is retained the choice of antibiotics has always been a point of discussion. Traditionally, patients receive pathogen specific antibiotics for 4-6 weeks between the first and second stage of surgery. Some centers report good outcome with just oral antibiotics.(181)

The risk factors for failure or reinfection after two stage exchange arthroplasty are lymphedema after TKA infection,(182) presence of a sinus tract,(183,184) previous revision surgery(185) and Rheumatoid arthritis.(185) Culture negative

PJI and infection with MRSA are associated with higher chance of reinfection.(184)

Treatment with Cefazolin(182) and use of antibiotic loaded PMMA have shown to have a low rate of reinfection.(186)

Two stage exchange arthroplasty is reported to be successful in 87-100% in revision THA(187,188) and 72-95% in revision TKA.(182,189,190) Two stage exchange or excision arthroplasty is found to be effective in fungal PJI.(94,96) Culture negative PJI treated with two stage exchange has shown the best results.(101)

Infection after a two stage exchange arthroplasty can be due to a preexisting infection or a new infection. Zmistowski et al showed that 2/3 of infections after two stage exchange are due to new infections and not relapse.(191) The median time of infection after a two stage revision was 9 months to three years and gram positive organisms were frequently implicated as the cause.(182,191)

## EXCISION ARTHROPLASTY

Excision arthroplasty is reserved as a salvage procedure to avoid amputation after failed attempts to control or eradicate PJI. Excision arthroplasty is done in patients who have undergone multiple procedures for PJI that failed, significant morbidity, and in those who were planned for a two stage revision but had significant perioperative complications. Patients might have a static or

articulating left there indefinitely. Patients with an articulating spacer have a better functional outcome when compared to the static spacers. It is more successful after failed THA where girdlestone arthroplasty(192) can be performed when compared to the knee joint after failed TKA. Girdlestone arthroplasty leads to a high rate of infection control and reduction in pain(193) but results in significant limb length discrepancies and patients might require help to ambulate. However, a reimplantation can be done at a later stage if deemed necessary. Antibiotic protocol is similar to two stage exchange with 4-6 weeks of intravenous antibiotic administration. Long term suppressive antibiotics might be required in some patients.

## ARTHRODESIS

Arthrodesis is another salvage procedure that is more commonly performed after a failed knee arthroplasty and rarely after a failed THA. Though some patients have the ability to ambulate following resection arthroplasty of the knee,(194) arthrodesis improves the mechanical stability. Arthrodesis can be performed using an intramedullary device or using an external fixator. The antibiotic protocol is similar to resection arthroplasty but patients who develop infected non union after arthrodesis might require a prolonged course of suppressive antibiotics.

## AMPUTATION

Amputation is a last resort and is reserved for patients who have failed all other modalities of treatment for PJI(195) or in patients who have life threatening infections where emergency control of infection is warranted.(196) Sierra et al published amputation as a rare outcome in 0.1% of patients.(195) However, a metaanalysis showed that 14%-25% of patients who had a failed two stage revision following infected TKA eventually underwent amputation.(182,197)

Antibiotic administration after amputation depends on whether all infected and necrotic tissue is removed. If the level of amputation or disarticulation is separate from infection, then a short term of antibiotics will suffice. However, in conditions where a long femoral stem was utilized or when there is acetabular osteomyelitis a longer term of antibiotics might be necessary and treatment will have to resemble treatment of chronic osteomyelitis.(44)

## LONG TERM SUPPRESSIVE ANTIBIOTICS

Long term suppressive antibiotics may be used as a treatment modality in a small subset of patients for treatment of PJI. It is usually reserved for patients who have multiple comorbid illness and might not be able to tolerate even a single surgical procedure. It has also been tried in patients with infection by a low virulent organism that is susceptible to oral antibiotics. Such a strategy is more effective in acute infections than in chronic or late infections.(198)

The optimal treatment with non-surgical options is unknown. Patients often receive 4-6 weeks of pathogen specific intravenous antibiotics or oral antibiotics with high bioavailability. Most patients are placed on long term or indefinite oral antibiotics.

## NOVEL ANTIBIOTIC DEVELOPMENT IN PJI

- Daptomycin is a lipopeptide with good gram positive coverage. A clinical trial with use of Daptomycin at 6 and 8 mg/kg for 6 weeks was found to be effective in treating staphylococcal PJI (MRSA) after a two stage revision.(199)
- Linezolid is an oxazolidinone that is very effective against gram positive organisms that are resistant like Methicillin resistant *staphylococcus* and Vancomycin resistant *enterococcus*.(200) Linezolid has emerged as an acceptable antibiotic for treatment of resistant organisms.
- Ceftaroline is an advanced cephalosporin with good activity against MRSA. Research is currently underway regarding its potential use in PJI.(201)

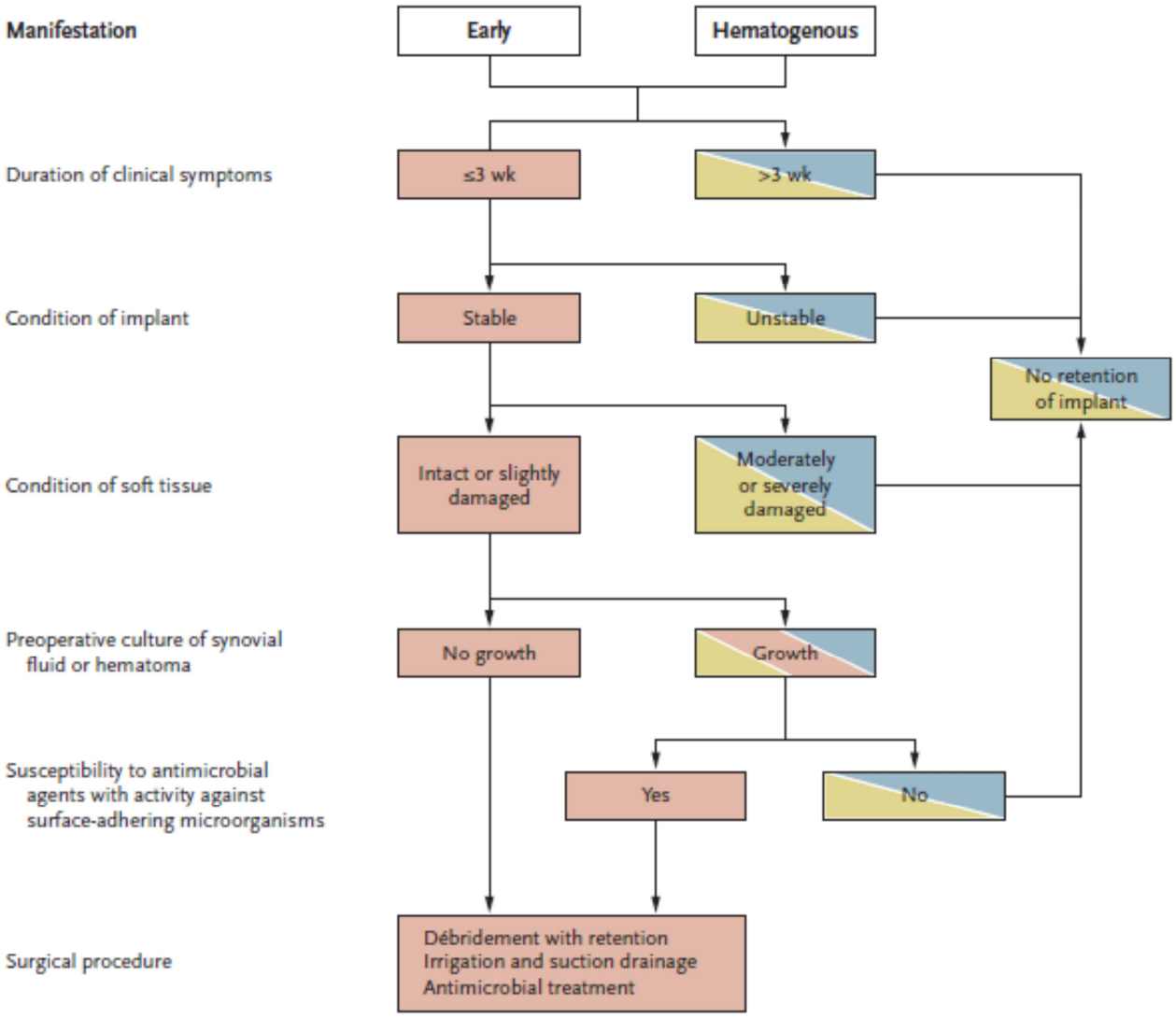



Fig.6 Algorithm for treatment of early or hematogenous infection(57)

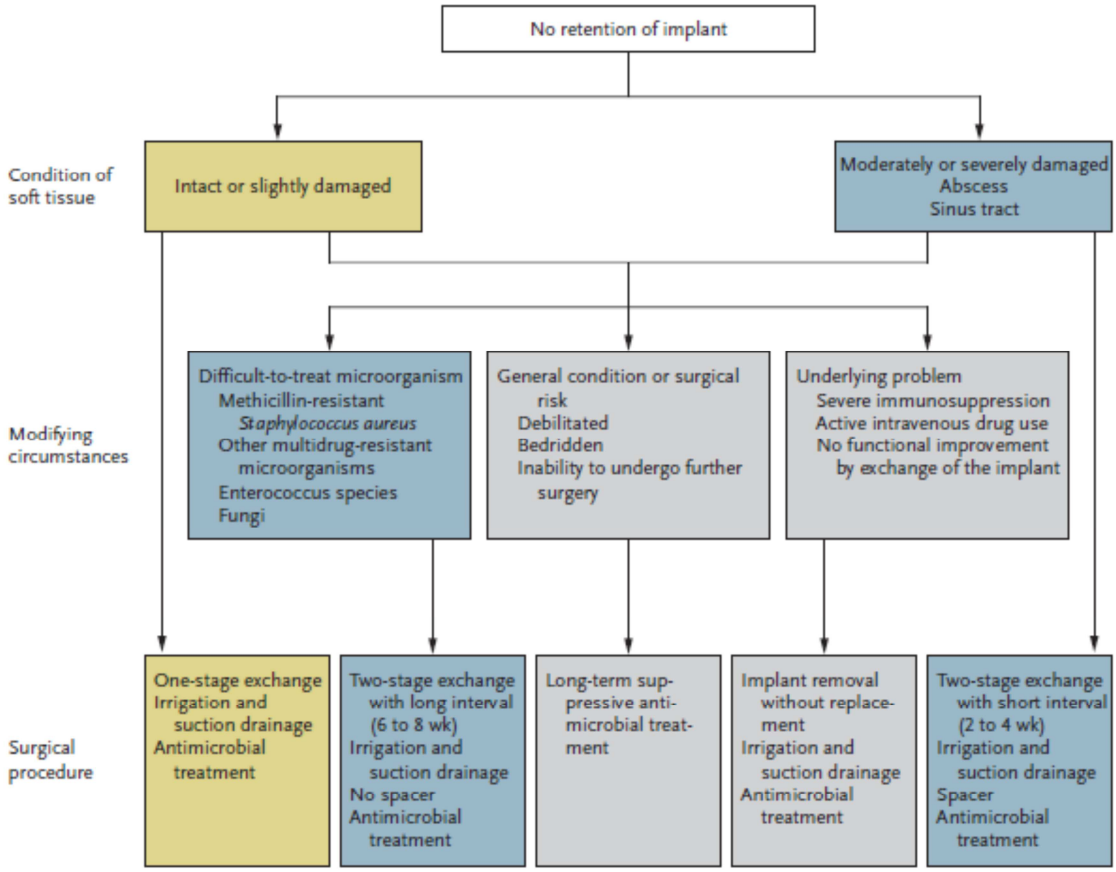



Fig.7 Algorithm for treatment when implant retention is not possible(57)

# PREVENTION OF PROSTHETIC JOINT INFECTIONS

Prevention of prosthetic joint infections has grown as an area of interest in recent times. There are several methods of prevention at various levels in patient care.

PREOPERATIVE METHODS

- Reduction of skin flora by adequate preparation preoperatively
- Perioperative antibiotics
- Preprocedure antibiotics prior to Dental, Gastrointestinal and Genitourinary procedures
- Vaccination against organisms causing PJI
- Control of Risk factors

INTRAOPERATIVE METHODS

- Laminar airflow and body exhaust suits
- Antibiotic loaded PMMA for implant placement

IMPLANT MODIFICATION TECHNIQUES(157)

- Nanodiamond particles to prevent adhesion of bacteria to implant surface
- Controlled release agents
- Antibiotic elution from titanium nanotubes
- Modification of implant surface by silver coating
- Anchoring antibiotics to implant surface

# LACUNAE IN CURRENT KNOWLEDGE

There has been significant research in the field of Prosthetic joint infections over the past two decades with significant improvement in a multitude of areas like diagnosis, identification of organisms, culture media, treatment modalities and choice of antibiotics. However, there has been a changing trend in organisms that cause infections worldwide especially in the surgical field. There is adequate literature available regarding outcomes with relation to treatment failure and success rates.

We have noticed a recent change in the profile of organisms that cause infections in Orthopaedics and hence would like to explore the change in profile of organisms that cause PJI. Furthermore, functional outcome of patients and the impact of PJI on regular activities of daily living have not been adequately studied. Hence, we have decided to identify and analyze these aspects of Prosthetic joint infections in a single center setting.

# MATERIALS AND METHODS

## STUDY DESIGN

The study was prospective follow up of retrospective cohorts. Over the past few years we have been noticing a general shift in the pattern of organisms that cause orthopaedic infections. We wish to evaluate if the same held true for arthroplasty infections. We chose two cohorts to compare the change in infection pattern over a period of five years. We conducted the study to compare two retrospective cohorts from 01.01.2007 – 31.12.2009 and 01.01.2012 – 31.12.2014.

Data regarding culture proven infections in Orthopaedics during the study period were obtained from the department of microbiology. A total of 8065 culture proven orthopaedic infections were identified. The data was analyzed and 150 PJI were identified. Of the 150, 116 were infections following THA and 33 were infections following TKA and one following Total elbow arthroplasty.

## SETTING

The study was conducted in Christian Medical College, Vellore which is a tertiary center. The study period was from 15.4.2015 – 15.4.2018. All patients who suffered from a culture proven arthroplasty infection were included in the study irrespective of the center where the index surgery was performed. The two retrospective cohorts mentioned above were recruited during the study

period. All the patients were contacted except the patients from other nationalities. The patients were invited for follow up and were examined and their functional outcome was assessed using the Modified Harris Hip Score for infected THA and the New Oxford Knee Score for infected TKA.

These patients were approached for recruitment into the study from the Department of Orthopaedics Unit I, II and III. An informed consent was obtained from all patients after completely explaining the procedure and clarifying queries.

INCLUSION CRITERIA

- All patients with a culture proven arthroplasty infection from 01.01.2007 – 31.12.2009 and 01.01.2012 – 31.12.2014 irrespective of the center where the index surgery was performed
- Any age group

EXCLUSION CRITERIA

- Tumour Megaprosthesis with infection
- Periprosthetic fractures associated with infection
- Patients unwilling to participate in the study

VARIABLES

The diagnostic criteria followed for diagnosing PJI was the criteria put forth by the International consensus group in 2014 which is as follows: (21)

Major Criteria: (One of the two)

- Sinus tract communicating with the prosthesis
- Same organism isolated on two or more separate cultures from the affected joint

Minor Criteria: (Three out of five)

- Elevated Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP)
- Elevated synovial fluid WBC count or ++ on leucocyte esterase strip
- Elevated synovial fluid neutrophil percentage (PMN %)
- Single positive culture
- More than 5 PMN/high power field (hpf) in 5 hpf during histopathological examination

The variables included were age, sex, religion, risk factors, number of hospitalizations, duration of hospitalization, loosening on Roentgenogram, microbiological culture, ESR, CRP, Synovial fluid counts, histopathology and type and duration of antibiotics.

## DATA SOURCE AND MEASUREMENT

Demographic data was obtained from the patient on history.

ESR and synovial fluid counts and histopathology data were obtained from the department of Clinical pathology, Christian Medical College, Vellore. The assessment of these data was according to the standard operating procedure of the department.

CRP and culture data was obtained from the department of Microbiology, Christian Medical College, Vellore. The assessment of these data was according to the standard operating procedure of the department.

Patients' Xrays were obtained from the department of Radiodiagnosis, Christian Medical College, Vellore.

## BIAS

Patients with prosthetic joint infections were examined by two orthopaedic surgeons to minimize interpersonal bias.

All arthroplasty infections during the study period were included in the study to minimize selection bias.

To minimize channeling bias, only culture proven cases were recruited.

All patients were prospectively followed up to minimize recall bias.

## DATA COLLECTION

Patients with culture proven prosthetic joint infection were identified with the data obtained from the Department of microbiology. The Inpatient and Outpatient records of the respective patients were accessed and contact numbers were obtained. All patients were contacted by the principal investigator and the patients were invited for follow up.

The details of the study were explained and all queries were clarified. An informed consent was obtained and the patients were examined and the data was entered in the proforma attached.

If the patients were unable to travel to the study center, results of Blood and Radiological investigations performed at a hospital in their hometown was obtained through electronic mail and the functional outcome was obtained over the phone.

The duration of data collection was from 18.2.2016 to 5.10.2017.

The patients were all identified from data obtained from the department of microbiology. A total of 150 patients were identified and were included in the study.

STATISTICAL METHODS

Data was entered using EPIDATA software and screened for outliers and extreme values using Box-Cox plot and histogram (for shape of the distribution). Summary of statistics was provided for reporting demographic and clinical characteristics. ANOVA was used to analyze continuous variable with culture. Chi-square performed for categorical variables with culture. Differences will be considered significant at $p<0.05$. All the statistical analysis was performed using SPSS 18.0.

This study was accepted by the Institutional Review Board, Christian Medical College,Vellore.

# RESULTS

The total number of patients identified for inclusion in the study was 150. Out of the 150 patients, 13patients were from outside the country and hence could not be contacted. 15 patients had expired due to multiple causes 55 people couldn't be contacted due to erroneous contact details. 2 patients had periprosthetic fractures and were excluded from the study and 7 patients refused to take part in the study. One patient had infection following elbow arthroplasty and was excluded from the study. This led to an attrition of 93 cases from the study and a total of 57 patients were invited to participate in the study. 24 patients responded and their details were collected and analyzed.

All patients who presented with a suspected PJI were evaluated for the infection and they underwent preliminary blood tests and Radiographs. A culture was taken if there was any discharge and was sent for analysis. Patients who had a well fixed implant on the plain radiograph, and mild rise of inflammatory markers with a relatively less virulent organism were given a trial of conservative management with implant retention but however, if there was persistence of symptoms, they underwent a surgical procedure.

Patients who had a loose implant on the plain radiograph and virulent organisms on culture were planned for revision surgery. Intraoperatively the joint space and tissues were examined and if there was a gross infection, debridement was performed and a cement spacer was placed and patients were subsequently planned for a two stage revision arthroplasty. If there was a high suspicion of infection but the joint was relatively well preserved, a frozen section was performed and if the histopathology was not suggestive of an active infection arthroplasty was done. Patients had a spacer placed if there was neutrophilic predominance on the histopathological report.

Patients who had persistent infection after multiple debridements and revision surgeries, underwent excision arthroplasty to eradicate the infection. We had one patient who suffered from persistent infection even after multiple debridements and long term suppressive antibiotics and required amputation as a last resort to eradicate the infection.

Out of the 24 patients assessed, 15 were male and the remaining 9 were female patients with ages ranging from 32 years to 82 years. The mean age was 56.42 with a median age of 56 and a standard deviation of 12.448. Patients were included from all three units of Orthopaedics in the institution. 16 out of 24 patients had their index surgery in CMC whereas the remaining 8 had their index surgery elsewhere. The total number of admissions to the hospital varied from 1 to 4 and the duration of admission varied from 8-126 days with a mean duration of 37.5 days and median of 31.5 days with a standard deviation of 27.67 days.

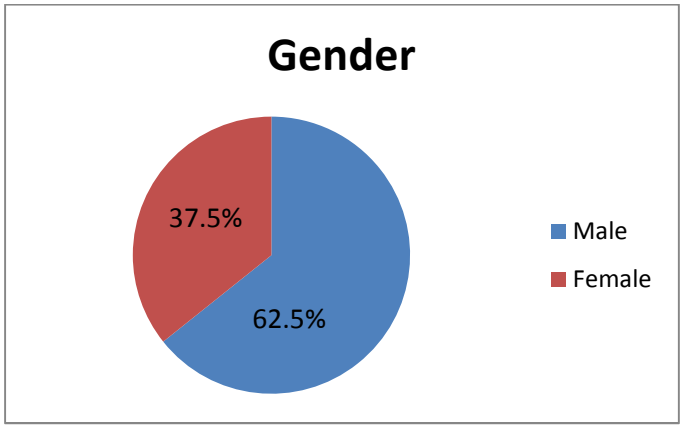



Figure 8 – Gender distribution

| | |
|---|---|
| Minimum Age | 32 |
| Maximum Age | 82 |
| Mean Age | 56.42 (32-82) |
| Median Age | 56 (32-82) |
| Standard Deviation | 12.45 |

Table 1 – Age Distribution

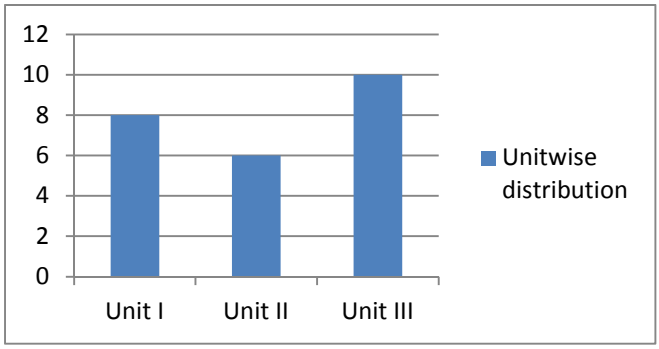



Figure 9 – Unitwise Distribution

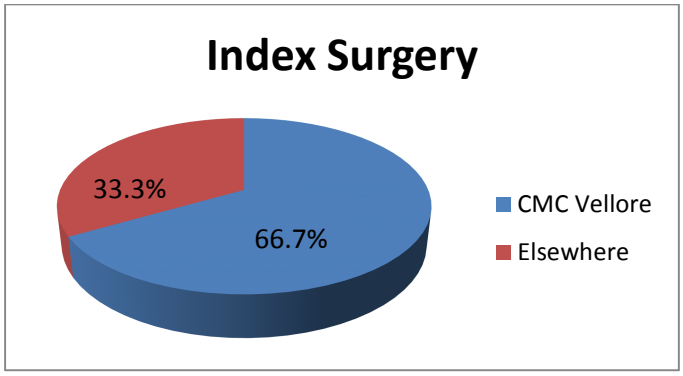



Figure 10 – Index Surgery

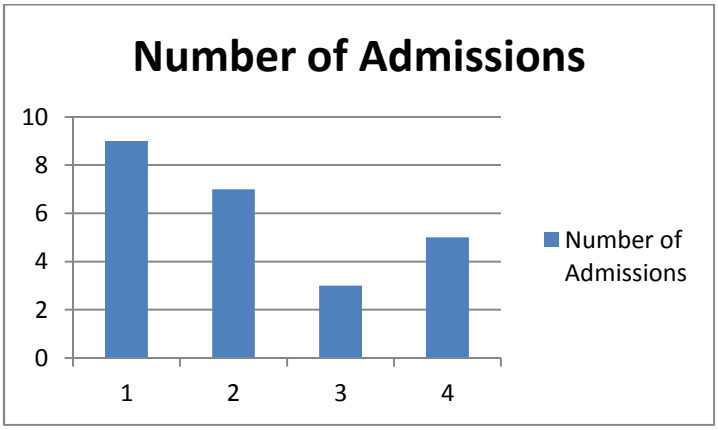



Figure 11 – Number of admissions

| | |
|---|---|
| Minimum Duration | 8 |
| Maximum Duration | 126 |
| Mean Duration | 37.5 (8-126) |
| Median Duration | 31.5 (8-126) |
| Standard Deviation | 27.67 |

Table 2 – Duration of admissions

16 patients out of the 24 underwent some form of arthroplasty for the hip and the remaining 8 underwent knee arthroplasty. In the 16 patients who underwent arthroplasty of the hip, 7 underwent Total hip replacement, 5 underwent bipolar hemiarthroplasty and 4 underwent revision arthroplasty. 3 out of 16 hips were cemented and the rest was uncemented.

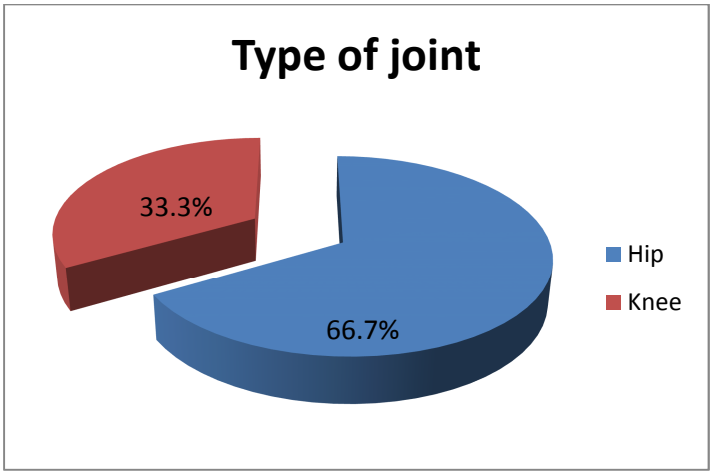



Figure 12 – Type of joint

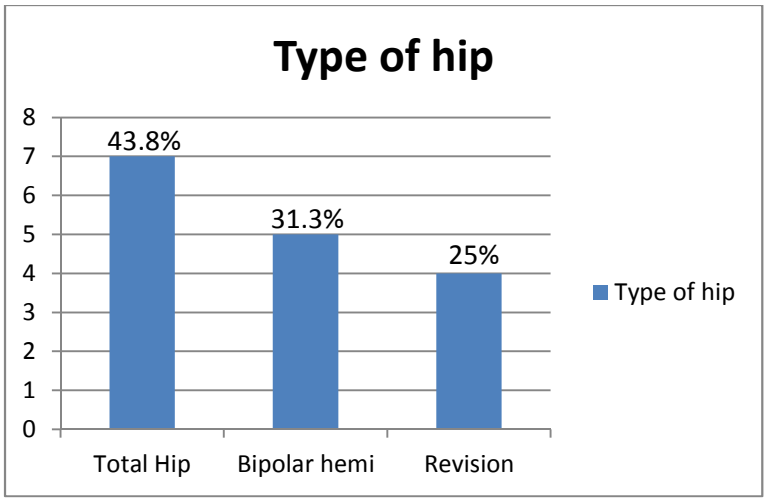



Figure 13 – Type of hip

A detailed table with the culture report is presented below and it reveals that of the infections, 8 were *Staphylococcus aureus*, 4 were Gram Negative Bacilli (GNB), 6 were Coagulase Negative *Staphylococcus aureus*, 4 were Enterococcus, 1 was β hemolytic streptococcus and 1 was a chronic infection due to Mycobacterium tuberculosis that had a superadded infection with GNB.

| Hospital No. | Organism 1 | Organism 2 | Organism 3 |
|---|---|---|---|
| 191181d | MRSA | - | - |
| 022611c | Entercoccus | - | - |
| 344605f | MRSA | - | - |
| 820811f | MRSA | - | - |
| 683209d | MRSA | - | - |
| 996835d | CONS (MR) | - | - |
| 702399c | ESBL | ESBL | ESBL |
| 450261f | Enterococcus | Enterococcus | - |
| 906379c | MRSA | MRSA | - |
| 562051c | CONS (MR) | - | - |
| 031434g | CONS (MR) | - | - |
| 301527d | CONS (MR) | - | - |
| 202627f | CONS (MR) | CONS (MR) | - |
| 157474c | Enterococcus | - | - |
| 564980g | ESBL | - | - |
| 704760c | CONS (MS) | - | - |
| 679074d | MSSA | MSSA | - |
| 462980f | M.Tuberculosis | ESBL | ESBL |
| 830828b | Enterococcus | MRSA | MRSA |
| 976250d | ESBL | ESBL | - |
| 863002f | GNB (Pan Sensitive) | - | - |
| 350008a | MSSA | MSSA | - |
| 991774g | MRSA | - | - |
| 014526d | β Hemolytic Streptococcus | β Hemolytic Streptococcus | - |

Table 3 – Detailed Culture report

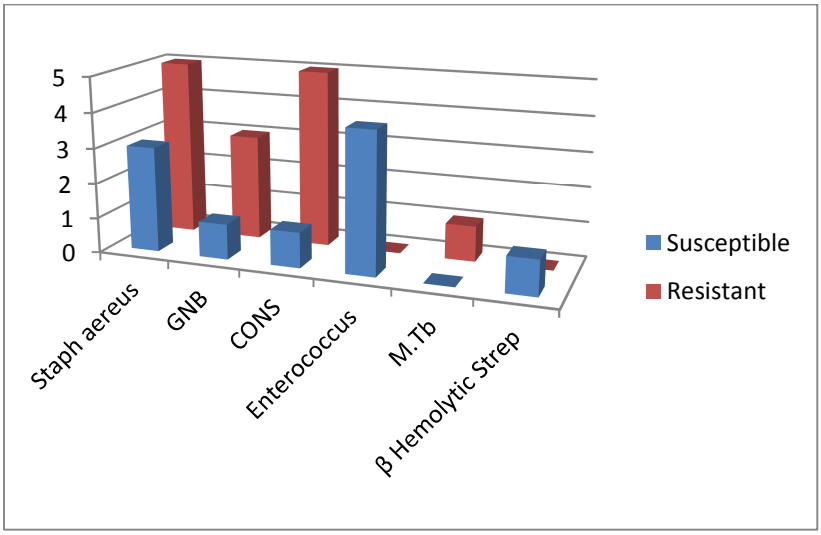



Figure 14 – Organisms identified

A draining sinus was present in 7 patients and the diagnosis of PJI was made on the basis of culture and blood tests in the remaining 17 patients.

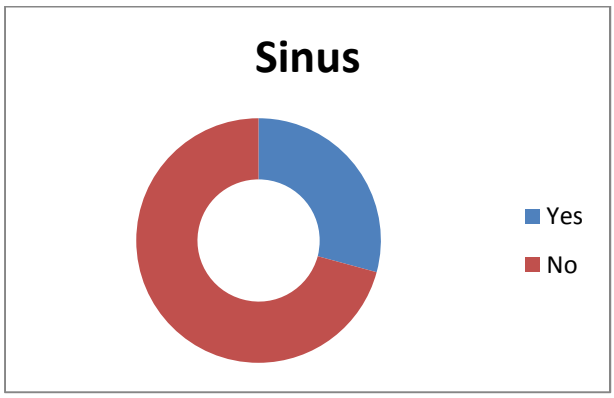



Figure 15 – Presence of sinus

9 patients fell in the first cohort that was from 2007-2009 and 15 patients were rom the second cohort from 2012-2014. Four prosthesis failed and 5 survived

in the first cohort and there was a survival of 5 prosthesis in the second cohort with 10 failures.

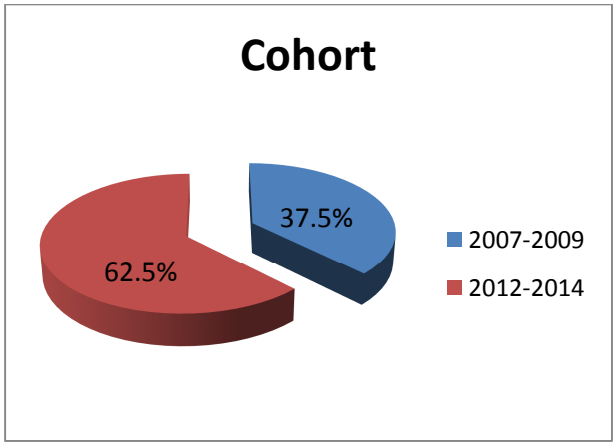



Figure 16 – Study cohorts

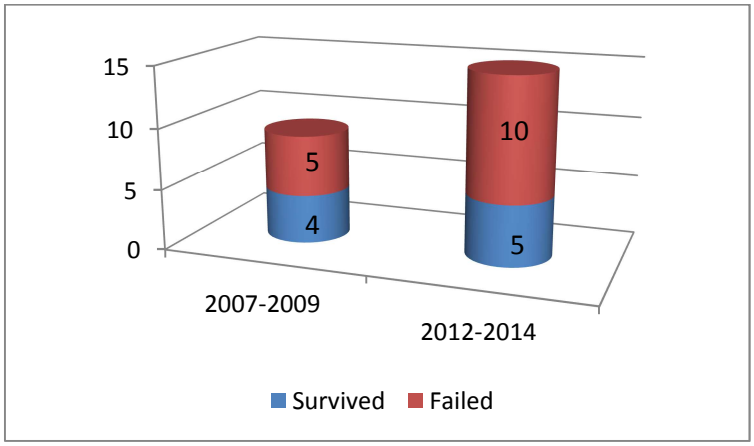



Figure 17 – Outcome based on cohorts

A total of 6 hips survived and 10 failed during the entire study period while 3 knees survived and 5 failed. All the 3 cemented hips failed whereas 6 out of 13 non cemented hips survived.

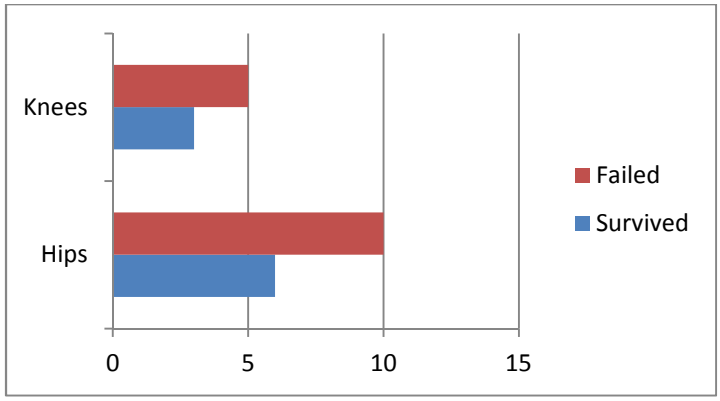



Figure 18 – Outcome of Prosthesis

The following table shows a detailed breakdown of the various outcomes of the prosthesis.

| Outcome | Number | Percentage |
|---|---|---|
| Survived | 9 | 37.5 |
| Failed | 16 | 62.5 |

Table 4 – Outcome of prosthesis

The following table depicts the various failures that occurred to the prosthesis during the study period.

| Outcome | Number | Percentage |
|---|---|---|
| One stage Revision | 2 | 8.3 |
| Two stage revision | 7 | 29.2 |
| Resection arthroplasty | 3 | 12.5 |
| Amputation | 1 | 4.2 |
| Death | 2 | 8.3 |

Table 5 – Failures

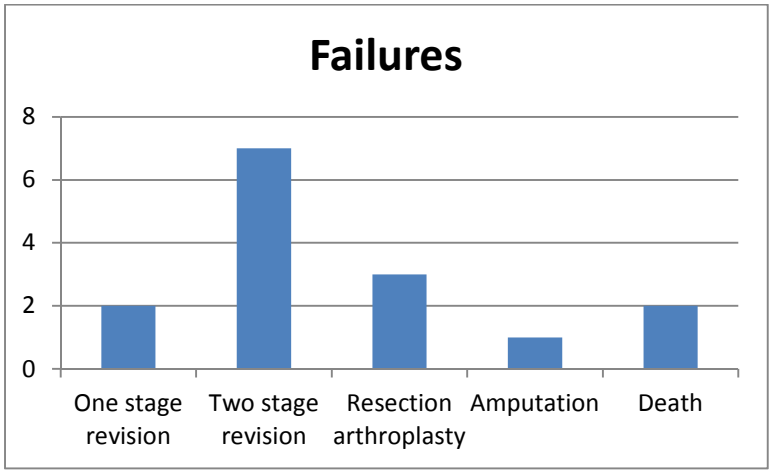



Figure 19 – Failures

There was a predisposition for infections by GNB in females and there was a definite increase in the number of infections caused by GNB in the second cohort but however, there was no significant difference in other organisms between the two cohorts.

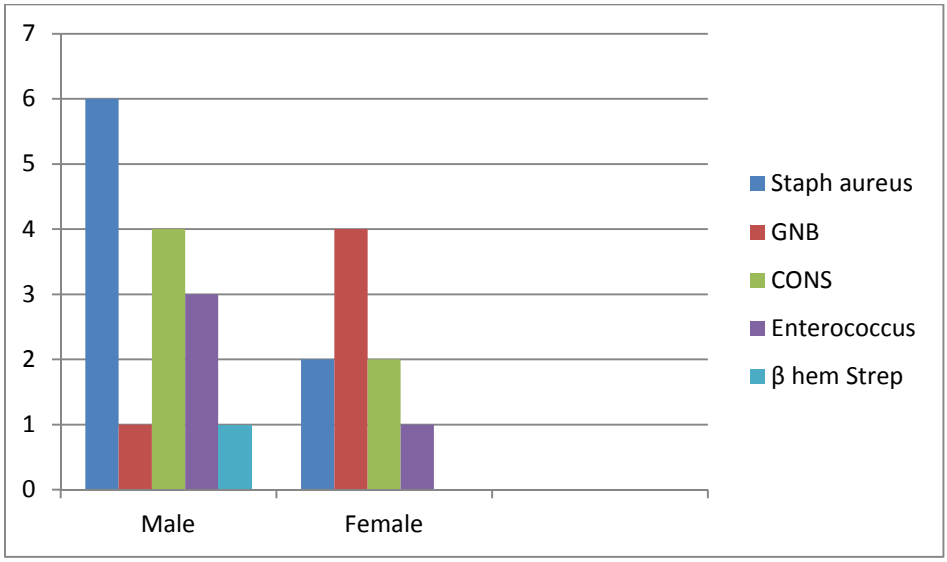



Figure 20 – Gender vs Organism

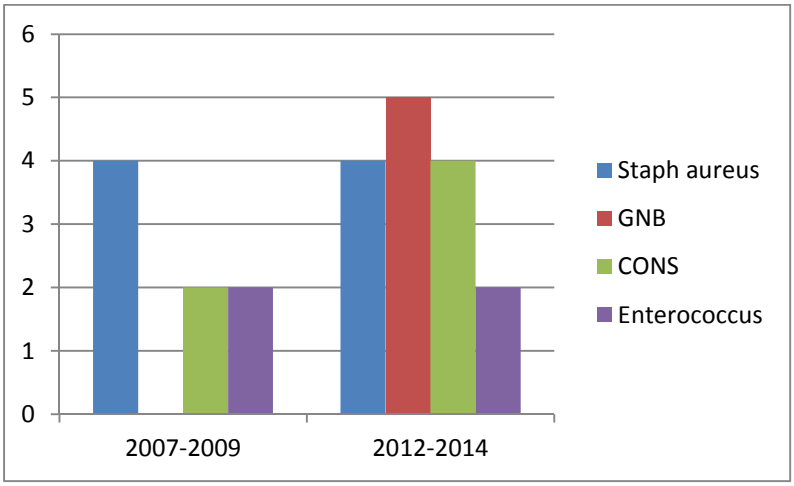



Figure 21 – Cohort vs Organism

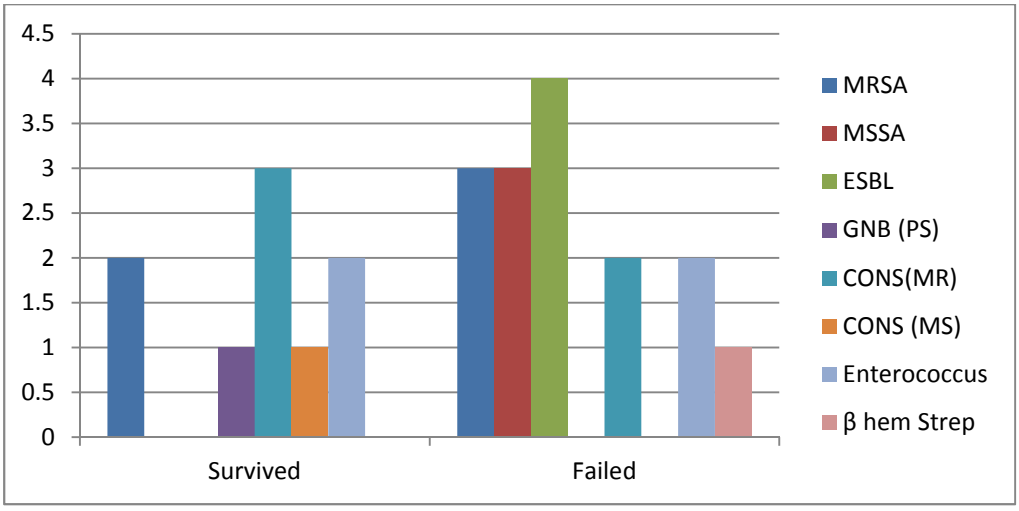



Figure 22 – Organism vs Outcome

| Outcome | Staph aureus | GNB | CONS | Enterococcus | β hemolytic Strep |
|---|---|---|---|---|---|
| Survived | 2 | 1 | 4 | 2 | 0 |
| One stage revision | 0 | 0 | 0 | 2 | 0 |
| Two stage revision | 4 | 1 | 2 | 0 | 0 |
| Resection arthroplasty | 2 | 1 | 0 | 0 | 0 |
| Amputation | 0 | 1 | 0 | 0 | 0 |
| Death | 0 | 1 | 0 | 0 | 1 |

Table 6 – Organism vs Outcome

Functional outcome in patients was analysed using New Oxford Knee Score and Modified Harris Hip Score. The details are depicted below.

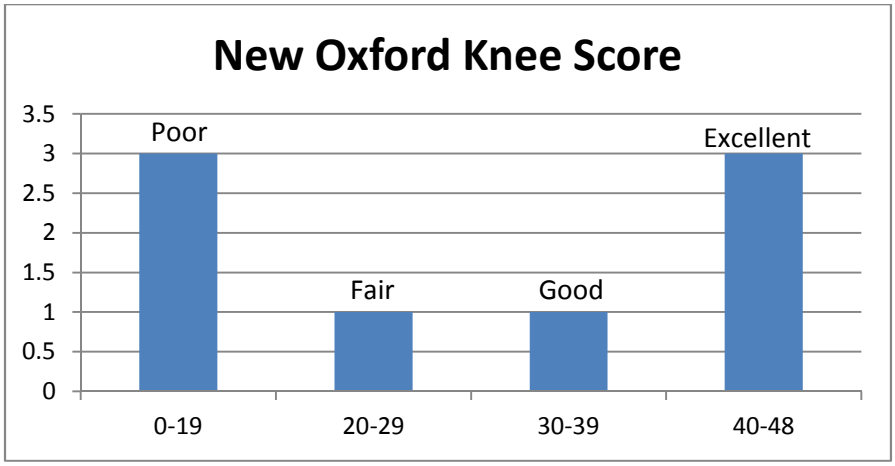



Figure 23 – Functional outcome after TKA

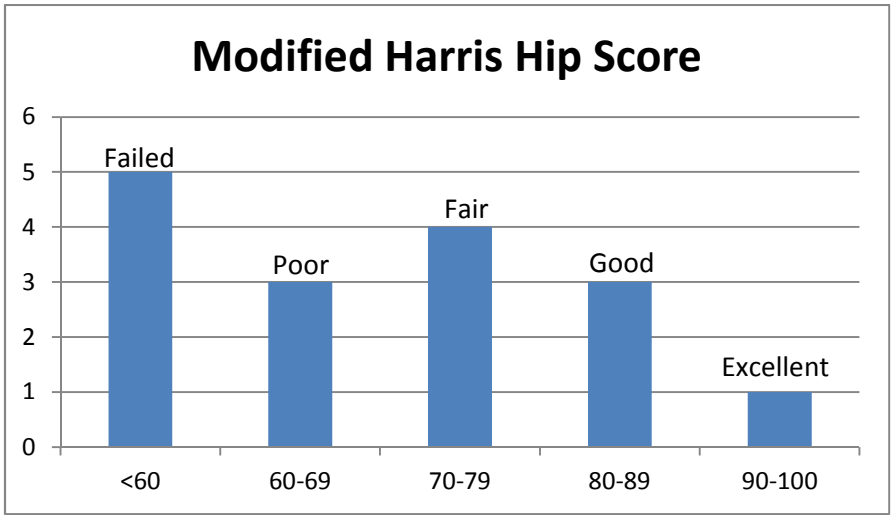



Figure 24 – Functional Outcome after THA

# RADIOGRAPHS


Figure 25 – Loosening of acetabular component


Figure 26 – Loosening of femoral component

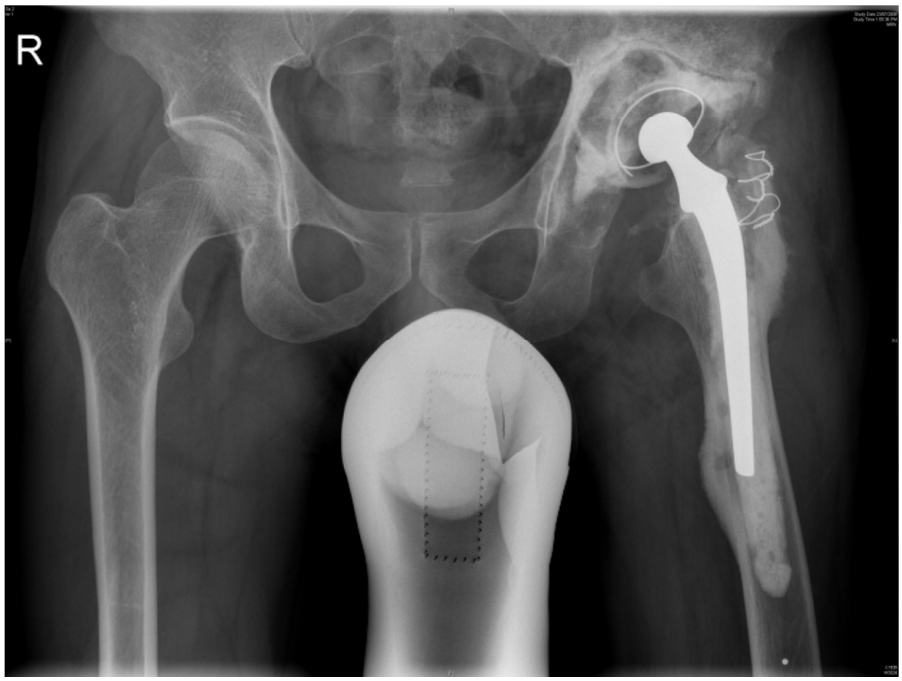



Figure 27 – Loosening of both acetabular and femoral component

Figure 28 – Loosening of tibial tray


Figure 29 – Single stage revision

Figure 30 – Antibiotic spacer as first stage in a two stage revision


Figure 31 – Second stage in a two stage revision

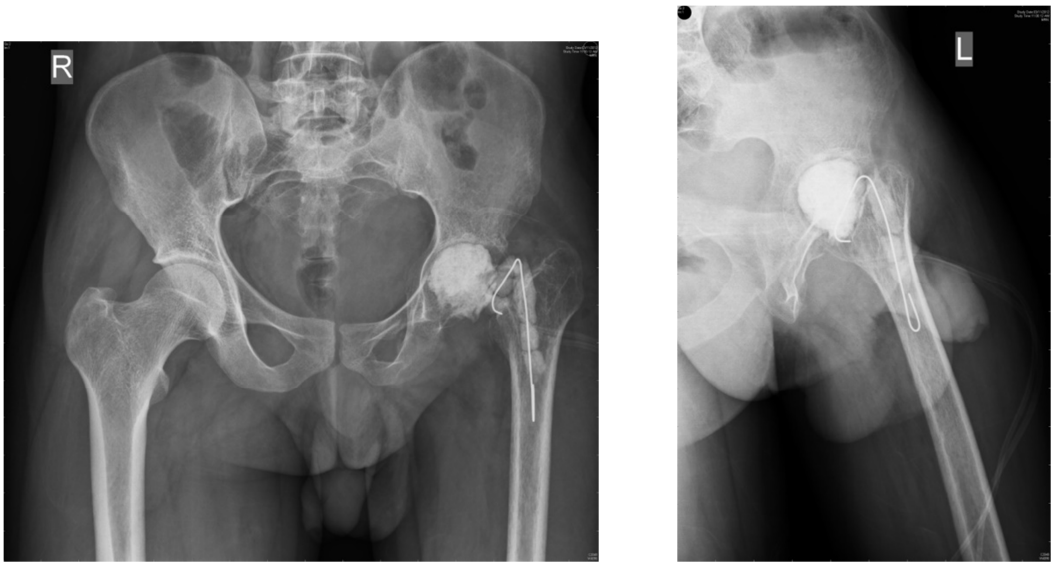



Figure 32 - Antibiotic spacer as first stage in a two stage revision


Figure 33 – Second stage in a two stage revision

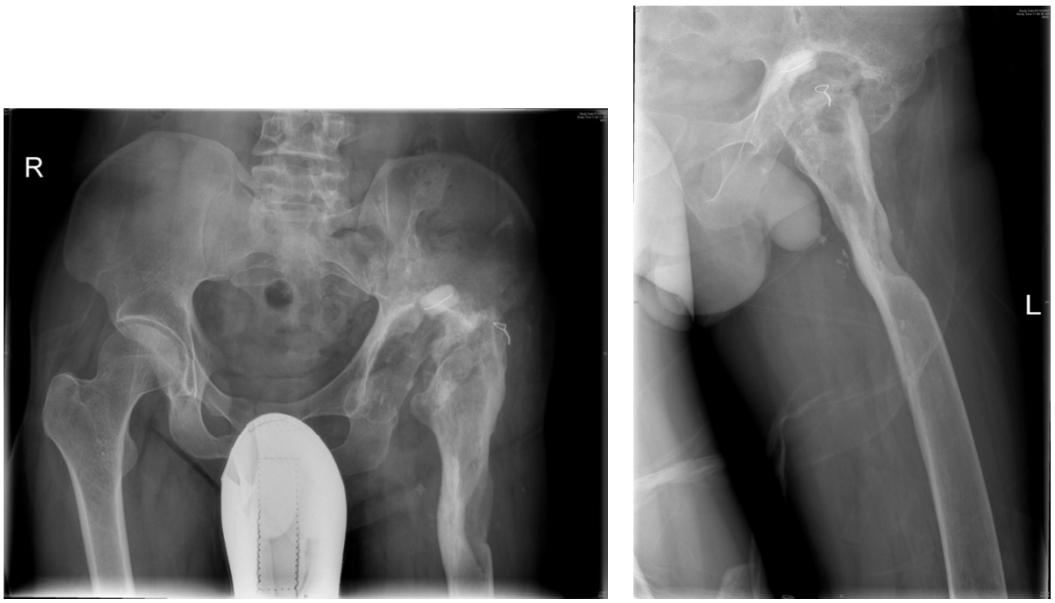



Figure 34 – Excision arthroplasty (Girdlestone arthroplasty)

# DISCUSSION

Periprosthetic joint infection is a devastating complication following a joint arthroplasty. Though, there are a lot of studies that have explored various diagnostic modalities and organisms implicated, there was a lacuna in the current knowledge on the outcomes of patients following PJI.

Hence, the study was designed to look at both the final outcome and current functional outcome in patients who had previously suffered from PJI.

Functional outcome was measured using two standardized scoring systems in use. We used the New Oxford Knee Score to assess functional outcome in patients who had TKA and the modified Harris Hip Score to assess functional outcome in patients who underwent arthroplasty of the hip.

In the study, we noticed that there was no difference between the age groups affected in terms of organism causing infection and also outcome. However, there was a significant increase in the duration and number of admissions in people who suffered PJI due to either MRSA or ESBL. ESBL had a longer median duration of admission with a median of 56 compared to 38 for MRSA.

All patients who presented with a suspected PJI were evaluated for the infection and they underwent preliminary blood tests and Radiographs. A culture was taken if there was any discharge and was sent for analysis. Patients who had a well fixed implant on the plain radiograph, and mild rise of inflammatory markers with a relatively less virulent organism were given a

trial of conservative management with implant retention but however, if there was persistence of symptoms, they underwent a surgical procedure.

Patients who had a loose implant on the plain radiograph and virulent organisms on culture were planned for revision surgery. Intraoperatively the joint space and tissues were examined and if there was a gross infection, debridement was performed and a cement spacer was placed and patients were subsequently planned for a two stage revision arthroplasty. If there was a high suspicion of infection but the joint was relatively well preserved, a frozen section was performed and if the histopathology was not suggestive of an active infection arthroplasty was done. Patients had a spacer placed if there was neutrophilic predominance on the histopathological report.

Patients who had persistent infection after multiple debridements and revision surgeries, underwent excision arthroplasty to eradicate the infection. We had one patient who suffered from persistent infection even after multiple debridements and long term suppressive antibiotics and required amputation as a last resort to eradicate the infection.

RETAINED IMPLANTS:

A total of 37.5% of prosthesis was retained and survived whereas 62.5% of people who suffered from PJI had failed implant and had to undergo revision surgery or some other salvage procedure.

The patients who had implant survival predominantly had infections caused by organisms of low virulence like CONS and Enterococcus (66.6%). Only 33.3%

of patients who had implant survival were affected by organisms of higher virulence. However, these 3 patients (2 infections were caused by *Staphylococcus aureus* and one by GNB) were sensitive to the first line of antibiotics and responded well to treatment with specific antibiotics.

SINGLE STAGE REVISIONS:

Two patients underwent a single stage revision arthroplasty and incidentally both of the patients had infections caused by enterococcus. Both the patients had infections caused by an organism of low virulence and had a relatively well preserved joint on intraoperative examination. Hence a decision was made to proceed with debridement and a single stage arthroplasty. However, on long term follow up they had a poor functional outcome. The modified Harris hip score was 65 and 66 for the two patients. It was also noticed that Enterococcus infections were more common after THA (75%) than TKA.

TWO STAGE REVISIONS:

Seven patients in the study group underwent two stage revision arthroplasty. Out of the seven, 4 infections were caused by Staphylococcus aureus and 2 by CONS and 1 by ESBL. Only two out of the seven had a good functional outcome and both were affected by organisms of low virulence. One infection was caused by CONS (modified Harris hip score of 82) and the other by MSSA (New oxford knee score of 38). All the other patients had a very poor outcome

on the long run. The patient who had infection caused by ESBL had the poorest outcome (modified Harris hip score of 8).

SALVAGE PROCEDURES:

Three patients underwent excision arthroplasty and two of them had infections caused by *Staphylococcus aureus* and one by ESBL. All three patients underwent multiple procedures to eradicate infection and had persistent infection. They underwent excision arthroplasty of the hip as a salvage procedure to eradicate the infection. However, they had a better functional outcome when compared to patients who had a single stage or a two stage revision. The modified Harris hip score in these patients was 78, 85 and 67. The two patients who had a fair and good outcome had infections caused by Staphylococcus aureus and the one with poor outcome following excision arthroplasty had infection caused by ESBL.

LOCAL MORBIDITY AND MORTALITY:

One patient underwent amputation as a last ditch effort to salvage a life threatening septic arthritis that was caused by ESBL. The patient had an initial infection with *Mycobacterium tuberculosis* and was on long term antituberculous therapy and subsequently developed septic arthritis that ultimately required amputation.

Two patients died from PJI and one had infection with ESBL and the other with β hemolytic streptococci.

OTHER FACTORS:

It was also noticed that patients who had infections due to ESBL predominantly belonged to the older age group (60-75) with ladies (80%) being affected more than the male population.

Though, there were more infections due to *Staphylococcus aureus*, with an even distribution in both cohorts, it was noticed that PJI due to ESBL as the causative organism was more frequent in the second cohort with all cases of PJI due to ESBL being implicated in the second cohort. This was in concordance with our hypothesis that there is indeed a change in the trend of organisms that cause PJI with more virulent and resistant organisms being implicated more recently.

The study revealed that PJI due to ESBL had a rather grim prognosis with more failures and more salvage procedures being performed to eradicate infection. From the results we can observe that infections caused by ESBL had the worst prognosis and also had a poorer outcome in patients who underwent revision arthroplasty.

ESBL is increasingly common in the older age group and was observed to affect female patients more often than male patients. Female patients are also more prone for urinary tract infections and ESBL is being increasingly implicated as a major causative organism for the same. Hence, patients with

prosthetic joints need to be treated more aggressively with specific antibiotics if an infection by ESBL is suspected.

On follow up, 7 patients were found to have an elevated ESR and CRP. Of this, two patients underwent revision surgery with a two stage arthroplasty during the study period, one patient underwent an above knee amputation and one patient perished during the study period. The remaining three patients were known cases of connective tissue disorder and had a reasonably good functional outcome and no other findings (clinical and radiological) to suggest infection at present.

It was noticed that patients with a previously failed surgery had a poorer functional outcome. Patients who had undergone Girdlestone arthroplasty had a better functional outcome when compared to the other modalities for treatment of failed arthroplasty following infection.

Prosthetic joint infections are increasingly common and will increase in the future when the number of revision surgeries increase due to various causes. We noticed that prosthetic joint infections are associated with a rather poor outcome in the long run. The complete eradication of infection is indeed a challenge and more so when highly virulent organisms cause the infection. Hence, early and accurate diagnosis of PJI is of paramount importance and treatment should be tailored for each patient according to general condition and the extent of infection with a special emphasis on the causative organism.

# CONCLUSION

Our study shows that there is an increase in incidence of organisms with high virulence and resistance like extended spectrum β lactamase Gram Negative Bacilli causing Periprosthetic joint infections. There was a change in the trend of organisms causing infection noted over the two study cohorts.

We also found that these organisms are associated with more chance of implant failure with salvage surgeries being increasingly needed to eradicate infection.

The functional outcome was generally higher in patients where the implant was retained and the infection was only superficial whereas, the functional outcome was generally poor in failed implants with ESBL being associated with the poorest outcomes.

# LIMITATIONS

1. The study had retrospective identification of patients with prospective follow up of patients. There was a significant lacuna in the patient information available in our hospital records and hence a lot of patients could not be contacted for participation in the study.
2. Small Sample size: The above mentioned problem led to a small sample size and this led to difficulties in analyzing data. A larger sample size would have yielded sufficient data to obtain a clearer picture on the changing trends and other modalities.
3. Synovial fluid analysis was not performed in all patients as a routine method for diagnosing PJI and hence, we had to rely heavily on cultures for identification of cases.

# FUTURE RESEARCH SUGGESTIONS

Periprosthetic joint infection is an exciting area that will require extensive research before finalizing the modalities for accurate and less invasive diagnosis. A large multicenter prospective study of all the diagnostic modalities would help improve the diagnostic criteria and increase the accuracy of diagnosis.

The findings from our study that there is indeed a change in trend of organisms that are causing PJI is very interesting and further research would help us to change our outlook towards the cause of PJI and lead to newer antibiotic protocols. A large prospective study with regular follow up would yield a treasure trove of data in this regard.

# BIBLIOGRAPHY


1. Maradit Kremers H, Larson DR, Crowson CS, Kremers WK, Washington RE, Steiner CA, et al. Prevalence of Total Hip and Knee Replacement in the United States. J Bone Joint Surg Am. 2015 Sep 2;97(17):1386–97.

2. Hall MJ, DeFrances CJ, Williams SN, Golosinskiy A, Schwartzman A. National hospital discharge survey: 2007 summary. US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics; 2010.

3. Stockley I. Infected Arthroplasty. J Trauma Orthop. 2014;2(3):52–3.

4. Charnley J, Eftekhar N. Postoperative infection in total prosthetic replacement arthroplasty of the hip-joint with special reference to the bacterial content of the air of the operating room. Br J Surg. 1969 Sep 1;56(9):641–9.

5. Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J. Economic burden of periprosthetic joint infection in the United States. J Arthroplasty. 2012 Sep;27(8 Suppl):61–65.e1.

6. Pulido L, Ghanem E, Joshi A, Purtill JJ, Parvizi J. Periprosthetic Joint Infection: The Incidence, Timing, and Predisposing Factors. Clin Orthop. 2008 Jul;466(7):1710–5.

7. Kuiper JWP, van den Bekerom MPJ, van der Stappen J, Nolte PA, Colen S. 2-stage revision recommended for treatment of fungal hip and knee prosthetic joint infections. Acta Orthop. 2013 Dec;84(6):517–23.

8. Parvizi J, Jacovides C, Zmistowski B, Jung KA. Definition of Periprosthetic Joint Infection: Is There a Consensus? Clin Orthop. 2011 Nov;469(11):3022–30.

9. Lamagni T. Epidemiology and burden of prosthetic joint infections. J Antimicrob Chemother. 2014 Sep;69 Suppl 1:i5-10.

10. Kurtz SM, Lau E, Schmier J, Ong KL, Zhao K, Parvizi J. Infection Burden for Hip and Knee Arthroplasty in the United States. J Arthroplasty. 2008 Oct;23(7):984–91.

11. Vanhegan IS, Malik AK, Jayakumar P, Islam SU, Haddad FS. A financial analysis of revision hip arthroplasty. J Bone Jt Surg Br. 2012;94(5):619–623.

12. Berbari EF, Osmon DR, Lahr B, Eckel-Passow JE, Tsaras G, Hanssen AD, et al. The Mayo prosthetic joint infection risk score: implication for surgical site infection reporting and risk stratification. Infect Control Hosp Epidemiol. 2012 Aug;33(8):774–81.

13. Spangehl MJ, Masri BA, O'connell JX, Duncan CP. Prospective analysis of preoperative and intraoperative investigations for the diagnosis of infection at the sites of two hundred and two revision total hip arthroplasties. J Bone Joint Surg Am. 81(5):672–83.

14. Parvizi J, Ghanem E, Menashe S, Barrack RL, Bauer TW. Periprosthetic infection: what are the diagnostic challenges? J Bone Joint Surg Am. 88 Suppl 4:138–47.

15. Trampuz A, Piper KE, Jacobson MJ, Hanssen AD, Unni KK, Osmon DR, et al. Sonication of removed hip and knee prostheses for diagnosis of infection. N Engl J Med. 2007;357(7):654–663.

16. Schinsky MF, Della Valle CJ, Sporer SM, Paprosky WG. Perioperative Testing for Joint Infection in Patients Undergoing Revision Total Hip Arthroplasty: J Bone Jt Surg-Am Vol. 2008 Sep;90(9):1869–75.

17. Parvizi J, Ghanem E, Sharkey P, Aggarwal A, Burnett RSJ, Barrack RL. Diagnosis of Infected Total Knee: Findings of a Multicenter Database. Clin Orthop. 2008 Nov;466(11):2628–33.

18. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care–associated infection and criteria for specific types of infections in the acute care setting. American journal of infection control. 2008 Jun 1;36(5):309-32.

19. Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, et al. Diagnosis and Management of Prosthetic Joint Infection: Clinical Practice Guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2013 Jan 1;56(1):e1–25.

20. Parvizi J, Zmistowski B, Berbari EF, Bauer TW, Springer BD, Della Valle CJ, et al. New Definition for Periprosthetic Joint Infection: From the Workgroup of the Musculoskeletal Infection Society. Clin Orthop. 2011 Nov;469(11):2992–4.

21. Parvizi J, Gehrke T, Chen AF. Proceedings of the International Consensus on Periprosthetic Joint Infection. Bone Jt J. 2013 Nov;95–B(11):1450–2.

22. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care–associated infection and criteria for specific types of infections in the acute care setting. American journal of infection control. 2008 Jun 1;36(5):309-32.

23. Jaberi FM, Parvizi J, Haytmanek CT, Joshi A, Purtill J. Procrastination of Wound Drainage and Malnutrition Affect the Outcome of Joint Arthroplasty. Clin Orthop. 2008 Jun;466(6):1368–71.

24. Marik PE. Surviving sepsis: going beyond the guidelines. Ann Intensive Care. 2011 Jun 7;1:17.

25. Moonen AF, Thomassen BJ, Knoors NT, van Os JJ, Verburg AD, Pilot P. Pre-operative injections of epoetin-α versus post-operative retransfusion of autologous shed blood in total hip and knee replacement. Bone & Joint Journal. 2008 Aug 1;90(8):1079-83.

26. Jämsen E, Huhtala H, Puolakka T, Moilanen T. Risk Factors for Infection After Knee Arthroplasty: A Register-Based Analysis of 43,149 Cases. J Bone Jt Surg-Am Vol. 2009 Jan;91(1):38–47.

27. Baek S-H. Identification and preoperative optimization of risk factors to prevent periprosthetic joint infection. World J Orthop. 2014 Jul 18;5(3):362–7.

28. Daines BK, Dennis DA, Amann S. Infection prevention in total knee arthroplasty. J Am Acad Orthop Surg. 2015 Jun;23(6):356–64.

29. Eka A, Chen AF. Patient-related medical risk factors for periprosthetic joint infection of the hip and knee. Ann Transl Med. 2015 Sep;3(16):233.

30. Berbari EF, Hanssen AD, Duffy MC, Steckelberg JM, Ilstrup DM, Harmsen WS, et al. Risk factors for prosthetic joint infection: case-control study. Clin Infect Dis. 1998;27(5):1247–1254.

31. Parvizi J, Ghanem E, Joshi A, Sharkey PF, Hozack WJ, Rothman RH. Does "Excessive" Anticoagulation Predispose to Periprosthetic Infection? J Arthroplasty. 2007 Sep;22(6):24–8.

32. Zevin S, Gourlay SG, Benowitz NL. Clinical pharmacology of nicotine. Clin Dermatol. 1998 Sep 1;16(5):557–64.

33. Shrader MW, Schall D, Parvizi J, McCarthy JT, Lewallen DG. Total Hip Arthroplasty in Patients With Renal Failure. J Arthroplasty. 2006 Apr 1;21(3):324–9.

34. Darouiche RO, Wall Jr MJ, Itani KM, Otterson MF, Webb AL, Carrick MM, et al. Chlorhexidine–alcohol versus povidone–iodine for surgical-site antisepsis. N Engl J Med. 2010;362(1):18–26.

36. Ritter MA. Operating room environment. Clinical orthopaedics and related research. 1999 Dec 1;369:103-9.

37. Salvati EA, Robinson RP, Zeno SM, Koslin BL, Brause BD, Wilson PD. Infection rates after 3175 total hip and total knee replacements performed with and without a horizontal unidirectional filtered air-flow system. J Bone Joint Surg Am. 64(4):525–35.

38. Willis-Owen CA, Konyves A, Martin DK. Factors affecting the incidence of infection in hip and knee replacement. Bone & Joint Journal. 2010 Aug 1;92(8):1128-33.

40. Fitzgerald Jr RH, Nolan DR, Ilstrup DM, Van Scoy RE, Washington 2nd JA, Coventry MB. Deep wound sepsis following total hip arthroplasty. JBJS. 1977 Oct 1;59(7):847-55.

41. Tsukayama DT, Estrada R, Gustilo RB. Infection after total hip arthroplasty. A study of the treatment of one hundred and six infections. J Bone Joint Surg Am. 78(4):512–23.

42. McPherson EJ, Woodson C, Holtom P, Roidis N, Shufelt C, Patzakis M. Periprosthetic total hip infection: outcomes using a staging system. Clin Orthop. 2002 Oct;(403):8–15.

43. Anagnostakos K, Schmid NV, Kelm J, Grün U, Jung J. Classification of hip joint infections. Int J Med Sci. 2009;6(5):227.

44. Tande AJ, Patel R. Prosthetic joint infection. Clin Microbiol Rev. 2014 Apr;27(2):302–45.

45. Southwood RT, Rice JL, McDonald PJ, Hakendorf PH, Rozenbilds MA. Infection in experimental hip arthroplasties. Bone & Joint Journal. 1985 Mar 1;67(2):229-31.

46. Gallo J, Kolar M, Novotny R, Rihakova P, Tichá V. Pathogenesis of prosthesis-related infection. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2003;147(1):27–35.

47. van Loosdrecht MC, Lyklema J, Norde W, Zehnder AJ. Influence of interfaces on microbial activity. Microbiol Rev. 1990 Mar;54(1):75–87.

48. Gristina AG, Naylor PT, Webb LX. Molecular mechanisms in musculoskeletal sepsis: the race for the surface. Instr Course Lect. 1990;39:471–82.

49. Taylor R, Maryan C, Verran J. Retention of oral microorganisms on cobalt-chromium alloy and dental acrylic resin with different surface finishes. J Prosthet Dent. 1998 Nov;80(5):592–7.

50. Donlan RM, Costerton JW. Biofilms: survival mechanisms of clinically relevant microorganisms. Clin Microbiol Rev. 2002 Apr;15(2):167–93.

51. Stoodley P, Nistico L, Johnson S, Lasko L-A, Baratz M, Gahlot V, et al. Direct demonstration of viable Staphylococcus aureus biofilms in an infected total joint arthroplasty. A case report. J Bone Joint Surg Am. 2008 Aug;90(8):1751–8.

52. Leid JG, Shirtliff ME, Costerton JW, Stoodley a. P. Human Leukocytes Adhere to, Penetrate, and Respond to Staphylococcus aureus Biofilms. Infect Immun. 2002 Nov 1;70(11):6339–45.

53. Belmatoug N, Crémieux AC, Bleton R, Volk A, Saleh-Mghir A, Grossin M, et al. A new model of experimental prosthetic joint infection due to methicillin-resistant Staphylococcus aureus: a microbiologic, histopathologic, and magnetic resonance imaging characterization. J Infect Dis. 1996 Aug;174(2):414–7.

54. Crémieux A-C, Carbon C. Experimental models of bone and prosthetic joint infections. Clin Infect Dis. 1997;25(6):1295–1302.

55. Peersman G, Laskin R, Davis J, Peterson M. Infection in total knee replacement: a retrospective review of 6489 total knee replacements. Clin Orthop. 2001 Nov;(392):15–23.

56. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a

prospective nationwide surveillance study. Clin Infect Dis Off Publ Infect Dis Soc Am. 2004 Aug 1;39(3):309–17.

57. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-Joint Infections. N Engl J Med. 2004 Oct 14;351(16):1645–54.

58. Ferry T, Uçkay I, Vaudaux P, François P, Schrenzel J, Harbarth S, et al. Risk factors for treatment failure in orthopedic device-related methicillin-resistant Staphylococcus aureus infection. Eur J Clin Microbiol Infect Dis Off Publ Eur Soc Clin Microbiol. 2010 Feb;29(2):171–80.

59. Sendi P, Rohrbach M, Graber P, Frei R, Ochsner PE, Zimmerli W. Staphylococcus aureus small colony variants in prosthetic joint infection. Clin Infect Dis. 2006;43(8):961–967.

60. Proctor RA, von Eiff C, Kahl BC, Becker K, McNamara P, Herrmann M, et al. Small colony variants: a pathogenic form of bacteria that facilitates persistent and recurrent infections. Nat Rev Microbiol. 2006 Apr;4(4):295–305.

61. Fey PD, Olson ME. Current concepts in biofilm formation of Staphylococcus epidermidis. Future Microbiol. 2010 Jun;5(6):917–33.

62. Vuong C, Dürr M, Carmody AB, Peschel A, Klebanoff SJ, Otto M. Regulated expression of pathogen-associated molecular pattern molecules in Staphylococcus epidermidis: quorum-sensing determines pro-inflammatory capacity and production of phenol-soluble modulins. Cell Microbiol. 2004 Aug;6(8):753–9.

63. Razonable RR, Lewallen DG, Patel R, Osmon DR. Vertebral osteomyelitis and prosthetic joint infection due to Staphylococcus simulans. Mayo Clin Proc. 2001 Oct;76(10):1067–70.

64. Allignet J, Galdbart JO, Morvan A, Dyke KG, Vaudaux P, Aubert S, et al. Tracking adhesion factors in Staphylococcus caprae strains responsible for human bone infections following implantation of orthopaedic material. Microbiol Read Engl. 1999 Aug;145 ( Pt 8):2033–42.

65. Sampathkumar P, Osmon DR, Cockerill FR. Prosthetic joint infection due to Staphylococcus lugdunensis. Mayo Clin Proc. 2000 May;75(5):511–2.

66. Diekema DJ, Pfaller MA, Schmitz FJ, Smayevsky J, Bell J, Jones RN, et al. Survey of infections due to Staphylococcus species: frequency of occurrence and antimicrobial susceptibility of isolates collected in the United States, Canada, Latin America, Europe, and the Western Pacific region for the SENTRY Antimicrobial Surveillance Program, 1997-1999. Clin Infect Dis Off Publ Infect Dis Soc Am. 2001 May 15;32 Suppl 2:S114-132.

67. Meehan AM, Osmon DR, Duffy MCT, Hanssen AD, Keating MR. Outcome of penicillin-susceptible streptococcal prosthetic joint infection treated with debridement and

retention of the prosthesis. Clin Infect Dis Off Publ Infect Dis Soc Am. 2003 Apr 1;36(7):845–9.

68. Zeller V, Lavigne M, Leclerc P, Lhotellier L, Graff W, Ziza JM, et al. Group B streptococcal prosthetic joint infections: a retrospective study of 30 cases. /data/revues/07554982/v38i11/S075549820900236X/ [Internet]. 2009 Sep 11 [cited 2017 Aug 24]; Available from: http://www.em-consulte.com/en/article/231231

69. J K, Gm G, Jm D. Group C streptococcal infection in a prosthetic joint. South Med J. 2000 Dec;93(12):1217–20.

70. Emerton ME, Crook DW, Cooke PH. Streptococcus bovis-infected total hip arthroplasty. J Arthroplasty. 1995;10(4):554–555.

71. Wollner A, Gilon D, Mattan Y, Rubinow A, Pogrund H. Pneumococcal infection of a prosthetic hip joint. Int Orthop. 1989 May 1;13(2):135–6.

72. Cunningham R, Walker C, Ridgway E. Prosthetic hip-joint infection associated with a penicillin-tolerant group B streptococcus. J Infect. 1992 Jul 1;25(1):77–81.

73. Cobo J, Miguel LGS, Euba G, Rodríguez D, García-Lechuz JM, Riera M, et al. Early prosthetic joint infection: outcomes with debridement and implant retention followed by antibiotic therapy. Clin Microbiol Infect. 2011 Nov 1;17(11):1632–7.

74. Aboltins CA, Dowsey MM, Buising KL, Peel TN, Daffy JR, Choong PFM, et al. Gram-negative prosthetic joint infection treated with debridement, prosthesis retention and antibiotic regimens including a fluoroquinolone. Clin Microbiol Infect. 2011 Jun 1;17(6):862–7.

75. Hsieh P-H, Lee MS, Hsu K-Y, Chang Y-H, Shih H-N, Ueng SW. Gram-negative Prosthetic Joint Infections: Risk Factors and Outcome of Treatment. Clin Infect Dis. 2009 Oct 1;49(7):1036–43.

76. Pottinger P, Butler-Wu S, Neradilek MB, Merritt A, Bertelsen A, Jette JL, et al. Prognostic Factors for Bacterial Cultures Positive for Propionibacterium acnes and Other Organisms in a Large Series of Revision Shoulder Arthroplasties Performed for Stiffness, Pain, or Loosening: J Bone Jt Surg-Am Vol. 2012 Nov;94(22):2075–83.

77. Shirwaiker RA, Springer BD, Spangehl MJ, Garrigues GE, Lowenberg DW, Garras DN, et al. A clinical perspective on musculoskeletal infection treatment strategies and challenges. J Am Acad Orthop Surg. 2015 Apr;23 Suppl:S44-54.

78. Piper KE, Jacobson MJ, Cofield RH, Sperling JW, Sanchez-Sotelo J, Osmon DR, et al. Microbiologic Diagnosis of Prosthetic Shoulder Infection by Use of Implant Sonication. J Clin Microbiol. 2009 Jun 1;47(6):1878–84.

79. Marculescu CE, Cantey JR. Polymicrobial Prosthetic Joint Infections: Risk Factors and Outcome. Clin Orthop. 2008 Jun 1;466(6):1397.

80. Bartz H, Nonnenmacher C, Bollmann C, Kuhl M, Zimmermann S, Heeg K, et al. Micromonas (Peptostreptococcus) micros: unusual case of prosthetic joint infection associated with dental procedures. Int J Med Microbiol. 2005 Jan 26;294(7):465–70.

81. Zaman R, Abbas M, Burd E. Late Prosthetic Hip Joint Infection with Actinomyces israelii in an Intravenous Drug User: Case Report and Literature Review. J Clin Microbiol. 2002 Nov 1;40(11):4391–2.

82. Peel TN, Cheng AC, Buising KL, Choong PFM. Microbiological Aetiology, Epidemiology, and Clinical Profile of Prosthetic Joint Infections: Are Current Antibiotic Prophylaxis Guidelines Effective? Antimicrob Agents Chemother. 2012 May 1;56(5):2386–91.

83. Zmistowski B, Fedorka CJ, Sheehan E, Deirmengian G, Austin MS, Parvizi J. Prosthetic Joint Infection Caused by Gram-Negative Organisms. J Arthroplasty. 2011 Sep 1;26(6):104–8.

84. Achermann Y, Trampuz A, Moro F, Wüst J, Vogt M. Corynebacterium bovis shoulder prosthetic joint infection: the first reported case. Diagn Microbiol Infect Dis. 2009 Jun 1;64(2):213–5.

85. Im T, Mo Q, M B, Mr S, A V. Corynebacterium jeikeium prosthetic joint infection: case report and literature review. Scand J Infect Dis. 2005;37(2):151–3.

86. Charlier C, Leclercq A, Cazenave B, Desplaces N, Travier L, Cantinelli T, et al. Listeria monocytogenes–Associated Joint and Bone Infections: A Study of 43 Consecutive Cases. Clin Infect Dis. 2012 Jan 15;54(2):240–8.

87. Brucellosis Cornplicating Bilateral Total Knee Arthroplasty. : Clinical Orthopaedics and Related Research [Internet]. LWW. [cited 2017 Aug 24]. Available from: http://journals.lww.com/corr/Fulltext/1991/06000/Brucellosis_Cornplicating_Bilateral_Total_Knee.28.aspx

88. Mehta H, Mackie I. Prosthetic joint infection with Pasturella multocida following cat scratch. J Arthroplasty. 2004 Jun 1;19(4):525–7.

89. Tande AJ, Cunningham SA, Raoult D, Sim FH, Berbari EF, Patel R. A Case of Q Fever Prosthetic Joint Infection and Description of an Assay for Detection of Coxiella burnetii. J Clin Microbiol. 2013 Jan 1;51(1):66–9.

90. Ef B, Ad H, Mc D, Jm S, Dr O. Prosthetic joint infection due to Mycobacterium tuberculosis: a case series and review of the literature. Am J Orthop Belle Mead NJ. 1998 Mar;27(3):219–27.

91. Spinner RJ, Sexton DJ, Goldner RD, Levin LS. Periprosthetic infections due to Mycobacterium tuberculosis in patients with no prior history of tuberculosis. J Arthroplasty. 1996 Feb 1;11(2):217–22.

92. Eid AJ, Berbari EF, Sia IG, Wengenack NL, Osmon DR, Razonable RR. Prosthetic Joint Infection Due to Rapidly Growing Mycobacteria: Report of 8 Cases and Review of the Literature. Clin Infect Dis. 2007 Sep 15;45(6):687–94.

93. Tierney M, Harris WH. Mycobacterium avium intracellulare infection of hip arthroplasties in an AIDS patient. Bone & Joint Journal. 1994 May 1;76(3):498-9.

94. Hwang B-H, Yoon J-Y, Nam C-H, Jung K-A, Lee S-C, Han C-D, et al. Fungal peri-prosthetic joint infection after primary total knee replacement. J Bone Jt Surg Br. 2012 May 1;94–B(5):656–9.

95. Jakobs O, Schoof B, Klatte TO, Schmidl S, Fensky F, Guenther D, et al. Fungal periprosthetic joint infection in total knee arthroplasty: a systematic review. Orthop Rev. 2015 Mar 3;7(1):5623.

96. Azzam K, Parvizi J, Jungkind D, Hanssen A, Fehring T, Springer B, Bozic K, Della Valle C, Pulido L, Barrack R. Microbiological, clinical, and surgical features of fungal prosthetic joint infections: a multi-institutional experience. JBJS. 2009 Nov 1;91(Supplement_6):142-9.

97. Austen S, van der Weegen W, Verduin CM, van der Valk M, Hoekstra HJ. Coccidioidomycosis Infection of a Total Knee Arthroplasty in a Nonendemic Region. J Arthroplasty. 2013 Feb 1;28(2):375.e13-375.e15.

98. Lackner M, De Man FH, Eygendaal D, Wintermans RGF, Kluytmans JA, Klaassen CH, et al. Severe prosthetic joint infection in an immunocompetent male patient due to a therapy refractory Pseudallescheria apiosperma. Mycoses. 2011 Oct 1;54:22–7.

99. David M P, Douglas R O, Arlen D H. Delayed reimplantation arthroplasty for candidal prosthetic joint infection: a report of 4 cases and review of the literature. Clinical Infectious Diseases. 2002 Apr 1;34(7):930-8.

100. Baumann PA, Cunningham B, Patel NS, Finn HA. Aspergillus fumigatus infection in a mega prosthetic total knee arthroplasty. J Arthroplasty. 2001 Jun 1;16(4):498–503.

101. Berbari EF, Marculescu C, Sia I, Lahr BD, Hanssen AD, Steckelberg JM, et al. Culture-Negative Prosthetic Joint Infection. Clin Infect Dis. 2007 Nov 1;45(9):1113–9.

102. Dowsey MM, Choong PFM. Obesity is a Major Risk Factor for Prosthetic Infection after Primary Hip Arthroplasty. Clin Orthop. 2008 Jan 1;466(1):153–8.

104. Biring GS, Kostamo T, Garbuz DS, Masri BA, Duncan CP. Two-stage revision arthroplasty of the hip for infection using an interim articulated Prostalac hip spacer: A 10-TO 15-YEAR FOLLOW-UP STUDY. Bone Jt J. 2009 Nov 1;91–B(11):1431–7.

105. Springer BD. The Diagnosis of Periprosthetic Joint Infection. J Arthroplasty. 2015 Jun 1;30(6):908–11.

106. Berbari E, Mabry T, Tsaras G, Spangehl M, Erwin PJ, Murad MH, Steckelberg J, Osmon D. Inflammatory blood laboratory levels as markers of prosthetic joint infection: a systematic review and meta-analysis. JBJS. 2010 Sep 1;92(11):2102-9.

107. White J, Kelly M, Dunsmuir R. C-reactive protein level after total hip and total knee replacement. J Bone Jt Surg Br. 1998;80(5):909–911.

108. Larsson S, Thelander UL, Friberg S. C-reactive protein (CRP) levels after elective orthopedic surgery. Clinical orthopaedics and related research. 1992 Feb 1;275:237-42.

109. Spangehl MJ, Masri BA, O'connell JX, Duncan CP. Prospective analysis of preoperative and intraoperative investigations for the diagnosis of infection at the sites of two hundred and two revision total hip arthroplasties. JBJS. 1999 May 1;81(5):672-83.

110. Ellitsgaard N, Andersson AP, Jensen KV, Jorgensen M. Changes in C-reactive protein and erythrocyte sedimentation rate after hip fractures. Int Orthop. 1991 Dec 1;15(4):311–4.

111. McArthur BA, Abdel MP, Taunton MJ, Osmon DR, Hanssen AD. Seronegative infections in hip and knee arthroplasty: periprosthetic infections with normal erythrocyte sedimentation rate and C-reactive protein level. Bone Jt J. 2015 Jul 1;97–B(7):939–44.

112. Della Valle C, Parvizi J, Bauer TW, DiCesare PE, Evans RP, Segreti J, Spangehl M, Watters III WC, Keith M, Turkelson CM, Wies JL. Diagnosis of periprosthetic joint infections of the hip and knee. Journal of the American Academy of Orthopaedic Surgeons. 2010 Dec 1;18(12):760-70.

113. Di Cesare PE, Chang E, Preston CF, Liu CJ. Serum interleukin-6 as a marker of periprosthetic infection following total hip and knee arthroplasty. JBJS. 2005 Sep 1;87(9):1921-7.

114. Bottner F, Wegner A, Winkelmann W, Becker K, Erren M, Götze C. Interleukin-6, procalcitonin and TNF-α: MARKERS OF PERI-PROSTHETIC INFECTION FOLLOWING TOTAL JOINT REPLACEMENT. Bone Jt J. 2007 Jan 1;89–B(1):94–9.

115. Ghanem E, Parvizi J, Burnett RSJ, Sharkey PF, Keshavarzi N, Aggarwal A, et al. Cell Count and Differential of Aspirated Fluid in the Diagnosis of Infection at the Site of Total Knee Arthroplasty: J Bone Jt Surg-Am Vol. 2008 Aug;90(8):1637–43.

116. Schinsky MF, Della Valle CJ, Sporer SM, Paprosky WG. Perioperative Testing for Joint Infection in Patients Undergoing Revision Total Hip Arthroplasty: J Bone Jt Surg-Am Vol. 2008 Sep;90(9):1869–75.

117. Ghanem E, Houssock C, Pulido L, Han S, Jaberi FM, Parvizi J. Determining “True” Leukocytosis in Bloody Joint Aspiration. J Arthroplasty. 2008 Feb 1;23(2):182–7.

118. Parvizi J, Jacovides C, Antoci V, Ghanem E. Diagnosis of Periprosthetic Joint Infection: The Utility of a Simple Yet Unappreciated Enzyme: J Bone Jt Surg-Am Vol. 2011 Dec;93(24):2242–8.

119. Aggarwal VK, Rasouli MR, Parvizi J. Periprosthetic joint infection: Current concept. Indian J Orthop. 2013 Jan;47(1):10–7.

120. Gram C. The differential staining of Schizomycetes in tissue sections and in dried preparations. Fortschitte Med. 1884;2:185–189.

121. Morgan PM, Sharkey P, Ghanem E, Parvizi J, Clohisy JC, Burnett RSJ, et al. The Value of Intraoperative Gram Stain in Revision Total Knee Arthroplasty: J Bone Jt Surg-Am Vol. 2009 Sep;91(9):2124–9.

122. Hazlett L, Wu M. Defensins in innate immunity. Cell Tissue Res. 2011 Jan 1;343(1):175–88.

123. Greenwald GI, Ganz T. Defensins mediate the microbicidal activity of human neutrophil granule extract against Acinetobacter calcoaceticus. Infect Immun. 1987 Jun 1;55(6):1365–8.

124. Agerberth B, Charo J, Werr J, Olsson B, Idali F, Lindbom L, et al. The human antimicrobial and chemotactic peptides LL-37 and α-defensins are expressed by specific lymphocyte and monocyte populations. Blood. 2000 Nov 1;96(9):3086–93.

125. Deirmengian C, Kardos K, Kilmartin P, Cameron A, Schiller K, Booth RE, et al. The Alpha-defensin Test for Periprosthetic Joint Infection Outperforms the Leukocyte Esterase Test Strip. Clin Orthop Relat Res. 2015 Jan 1;473(1):198–203.

126. Frangiamore SJ, Gajewski ND, Saleh A, Farias-Kovac M, Barsoum WK, Higuera CA. α-Defensin Accuracy to Diagnose Periprosthetic Joint Infection—Best Available Test? J Arthroplasty. 2016 Feb;31(2):456–60

127. Deirmengian C, Hallab N, Tarabishy A, Valle CD, Jacobs JJ, Lonner J, et al. Synovial Fluid Biomarkers for Periprosthetic Infection. Clin Orthop Relat Res. 2010 Aug 1;468(8):2017–23.

128. Jacovides CL, Parvizi J, Adeli B, Jung KA. Molecular Markers for Diagnosis of Periprosthetic Joint Infection. J Arthroplasty. 2011 Sep 1;26(6):99–103.e1.

129. Gollwitzer H, Dombrowski Y, Prodinger PM, Peric M, Summer B, Hapfelmeier A, et al. Antimicrobial Peptides and Proinflammatory Cytokines in Periprosthetic Joint Infection: J Bone Jt Surg. 2013 Apr;95(7):644–51.

130. Marin M, Garcia-Lechuz JM, Alonso P, Villanueva M, Alcalá L, Gimeno M, et al. The role of universal 16S rRNA gene PCR and sequencing in the diagnosis of prosthetic joint infection. J Clin Microbiol. 2011 Dec 14;JCM.00170-11.

131. Hughes HC, Newnham R, Athanasou N, Atkins BL, Bejon P, Bowler ICJW. Microbiological diagnosis of prosthetic joint infections: a prospective evaluation of four bacterial culture media in the routine laboratory. Clin Microbiol Infect. 2011 Oct 1;17(10):1528–30.

132. Butler-Wu SM, Burns EM, Pottinger PS, Magaret AS, Rakeman JL, Matsen FA, et al. Optimization of Periprosthetic Culture for Diagnosis of Propionibacterium acnes Prosthetic Joint Infection. J Clin Microbiol. 2011 Jul 1;49(7):2490–5.

133. Tigges S, Stiles RG, Roberson JR. Appearance of septic hip prostheses on plain radiographs. AJR Am J Roentgenol. 1994;163(2):377–380.

134. Miller TT. Imaging of hip arthroplasty. Eur J Radiol. 2012 Dec 1;81(12):3802–12.

135. Kitamura N, Leung SB, Engh Sr CA. Characteristics of pelvic osteolysis on computed tomography after total hip arthroplasty. Clinical orthopaedics and related research. 2005 Dec 1;441:291-7.

136. Sofka CM. Current applications of advanced cross-sectional imaging techniques in evaluating the painful arthroplasty. Skeletal Radiol. 2007 Mar 1;36(3):183–93.

137. Hayter CL, Koff MF, Shah P, Koch KM, Miller TT, Potter HG. MRI After Arthroplasty: Comparison of MAVRIC and Conventional Fast Spin-Echo Techniques. Am J Roentgenol. 2011 Sep 1;197(3):W405–11.

138. Cahir JG, Toms AP, Marshall TJ, Wimhurst J, Nolan J. CT and MRI of hip arthroplasty. Clinical radiology. 2007 Dec 31;62(12):1163-71.

139. Medicina Nucleare Unit, Ospedale S. Andrea, University of Rome “Sapienza”, Via di Grottarossa 1035, 00189 Roma, Italy, Glaudemans A, Galli F, Pacilio M, Signore A. Leukocyte and bacteria imaging in prosthetic joint infection. Eur Cell Mater. 2013 Jan 16;25:61–77.

140. Love C, Marwin SE, Tomas MB, Krauss ES, Tronco GG, Bhargava KK, et al. Diagnosing infection in the failed joint replacement: a comparison of coincidence detection 18F-FDG and 111In-labeled leukocyte/99mTc-sulfur colloid marrow imaging. J Nucl Med. 2004;45(11):1864–1871.

141. Kwee TC, Kwee RM, Alavi A. FDG-PET for diagnosing prosthetic joint infection: systematic review and metaanalysis. Eur J Nucl Med Mol Imaging. 2008 Nov;35(11):2122–32.

142. Zeller V, Ghorbani A, Strady C, Leonard P, Mamoudy P, Desplaces N. Propionibacterium acnes: An agent of prosthetic joint infection and colonization. J Infect. 2007 Aug 1;55(2):119–24.

143. Bori G, Soriano A, García S, Gallart X, Mallofre C, Mensa J. Neutrophils in frozen section and type of microorganism isolated at the time of resection arthroplasty for the treatment of infection. Arch Orthop Trauma Surg. 2009 May;129(5):591–5.

144. Mirra JM, Amstutz HC, Matos M, Gold R. The pathology of the joint tissues and its clinical relevance in prosthesis failure. Clinical orthopaedics and related research. 1976 Jun 1;117:221-40.

145. Janz V, Wassilew GI, Hasart O, Matziolis G, Tohtz S, Perka C. Evaluation of sonicate fluid cultures in comparison to histological analysis of the periprosthetic membrane for the detection of periprosthetic joint infection. Int Orthop. 2013 May;37(5):931–6.

146. Morawietz L, Classen R-A, Schröder JH, Dynybil C, Perka C, Skwara A, et al. Proposal for a histopathological consensus classification of the periprosthetic interface membrane. J Clin Pathol. 2006 Jun 1;59(6):591–7.

147. Tunney MM, Patrick S, Gorman SP, Nixon JR, Anderson N, Davis RI, et al. Improved detection of infection in hip replacements: A CURRENTLY UNDERESTIMATED PROBLEM. J Bone Jt Surg Br. 1998 Jul 1;80–B(4):568–72.

148. Trampuz A, Osmon DR, Hanssen AD, Steckelberg JM, Patel R. Molecular and antibiofilm approaches to prosthetic joint infection. Clinical orthopaedics and related research. 2003 Sep 1;414:69-88.

149. Esteban J, Gomez-Barrena E, Cordero J, Martín-de-Hijas NZ, Kinnari TJ, Fernandez-Roblas R. Evaluation of Quantitative Analysis of Cultures from Sonicated Retrieved Orthopedic Implants in Diagnosis of Orthopedic Infection. J Clin Microbiol. 2008 Feb 1;46(2):488–92.

150. Trampuz A, Piper KE, Hanssen AD, Osmon DR, Cockerill FR, Steckelberg JM, et al. Sonication of Explanted Prosthetic Components in Bags for Diagnosis of Prosthetic Joint Infection Is Associated with Risk of Contamination. J Clin Microbiol. 2006 Feb 1;44(2):628–31.

151. Kobayashi H, Oethinger M, Tuohy MJ, Procop GW, Bauer TW. Improved Detection of Biofilm-formative Bacteria by Vortexing and Sonication: A Pilot Study. Clin Orthop. 2009 May 1;467(5):1360–4.

152. Bergin PF, Doppelt JD, Hamilton WG, Mirick GE, Jones AE, Sritulanondha S, et al. Detection of Periprosthetic Infections With Use of Ribosomal RNA-Based Polymerase Chain Reaction. J Bone Joint Surg Am. 2010 Mar;92(3):654–63.

153. Matsen Ko L, Parvizi J. Diagnosis of Periprosthetic Infection: Novel Developments. Orthop Clin North Am. 2016 Jan;47(1):1–9.

154. Kobayashi H, Oethinger M, Tuohy MJ, Hall GS, Bauer TW. Improving clinical significance of PCR: Use of propidium monoazide to distinguish viable from dead staphylococcus aureus and staphylococcus epidermidis. J Orthop Res. 2009 Sep 1;27(9):1243–7.

155. Kobayashi N, Inaba Y, Choe H, Aoki C, Ike H, Ishida T, et al. Simultaneous Intraoperative Detection of Methicillin-Resistant Staphylococcus and Pan-Bacterial Infection During Revision Surgery: Use of Simple DNA Release by Ultrasonication and Real-Time Polymerase Chain Reaction. J Bone Jt Surg-Am Vol. 2009 Dec;91(12):2896–902.

156. Ecker DJ, Sampath R, Massire C, Blyn LB, Hall TA, Eshoo MW, et al. Ibis T5000: a universal biosensor approach for microbiology. Nat Rev Microbiol Lond. 2008 Jul;6(7):553–8.

157. Parvizi J, Alijanipour P, Barberi EF, Hickok NJ, Phillips KS, Shapiro IM, et al. Novel developments in the prevention, diagnosis, and treatment of periprosthetic joint infections. J Am Acad Orthop Surg. 2015 Apr;23 Suppl:S32-43.

158. Diaz-Ledezma C, Higuera CA, Parvizi J. Success after treatment of periprosthetic joint infection: a Delphi-based international multidisciplinary consensus. Clin Orthop. 2013 Jul;471(7):2374–82.

159. Mahmud T, Lyons MC, Naudie DD, MacDonald SJ, McCalden RW. Assessing the Gold Standard: A Review of 253 Two-Stage Revisions for Infected TKA. Clin Orthop Relat Res. 2012 Oct 1;470(10):2730–6.

160. Senneville E, Joulie D, Legout L, Valette M, Dezèque H, Beltrand E, et al. Outcome and Predictors of Treatment Failure in Total Hip/Knee Prosthetic Joint Infections Due to Staphylococcus aureus. Clin Infect Dis. 2011 Aug 15;53(4):334–40.

161. Tsukayama DT, Estrada R, Gustilo RB. Infection after total hip arthroplasty. A study of the treatment of one hundred and six infections. J Bone Joint Surg Am. 1996 Apr;78(4):512–23.

162. Raut VV, Siney PD, Wroblewski BM. One-Stage Revision of Total Hip Arthroplasty for Deep Infection. Clinical orthopaedics and related research. 1995 Dec 1;321:202-7.

163. Byren I, Bejon P, Atkins BL, Angus B, Masters S, McLardy-Smith P, et al. One hundred and twelve infected arthroplasties treated with 'DAIR' (debridement, antibiotics and implant retention): antibiotic duration and outcome. J Antimicrob Chemother. 2009 Jun 1;63(6):1264–71.

164. Marculescu CE, Berbari EF, Hanssen AD, Steckelberg JM, Harmsen SW, Mandrekar JN, et al. Outcome of Prosthetic Joint Infections Treated with Debridement and Retention of Components. Clin Infect Dis. 2006 Feb 15;42(4):471–8.

165. Koyonos L, Zmistowski B, Valle CJD, Parvizi J. Infection Control Rate of Irrigation and Débridement for Periprosthetic Joint Infection. Clin Orthop Relat Res. 2011 Nov 1;469(11):3043.

166. Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, et al. Diagnosis and Management of Prosthetic Joint Infection: Clinical Practice Guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2013 Jan 1;56(1):e1–25.

167. Leone S, Borrè S, Monforte A d'Arminio, Mordente G, Petrosillo N, Signore A, et al. Consensus document on controversial issues in the diagnosis and treatment of prosthetic joint infections. Int J Infect Dis. 2010 Oct 1;14:S67–77.

168. Silva M, Tharani R, Schmalzried TP. Results of direct exchange or debridement of the infected total knee arthroplasty. Clinical orthopaedics and related research. 2002 Nov 1;404:125-31.

169. Soriano A, García S, Bori G, Almela M, Gallart X, Macule F, et al. Treatment of acute post-surgical infection of joint arthroplasty. Clin Microbiol Infect. 2006 Sep 1;12(9):930–3.

170. Jaén N, Martínez-Pastor JC, Muñoz-Mahamud E, García-Ramiro S, Bosch J, Mensa J, Soriano A. Long-term outcome of acute prosthetic joint infections due to gram-negative bacilli treated with retention of prosthesis. Revista Española de Quimioterapia. 2012 Sep 1;25(3).

171. Azzam KA, Seeley M, Ghanem E, Austin MS, Purtill JJ, Parvizi J. Irrigation and Debridement in the Management of Prosthetic Joint Infection: Traditional Indications Revisited. J Arthroplasty. 2010 Oct 1;25(7):1022–7.

172. Ff B, Fp F, J D. Primary exchange revision arthroplasty for infected total knee replacement: a long-term study. Am J Orthop Belle Mead NJ. 2004 Apr;33(4):190–8; discussion 198.

173. Raut VV, Siney PD, Wroblewski BM. One-stage revision of infected total hip replacements with discharging sinuses. Bone Jt J. 1994 Sep 1;76–B(5):721–4.

174. Whiteside LA, Peppers M, Nayfeh TA, Roy ME. Methicillin-resistant Staphylococcus aureus in TKA treated with revision and direct intraarticular antibiotic infusion. Clinical Orthopaedics and Related Research®. 2011 Jan 1;469(1):26-33.

175. Cui Q, Mihalko WM, Shields JS, Ries M, Saleh KJ. Antibiotic-impregnated cement spacers for the treatment of infection associated with total hip or knee arthroplasty. JBJS. 2007 Apr 1;89(4):871-82.

176. Kalore NV, Maheshwari A, Sharma A, Cheng E, Gioe TJ. Is There a Preferred Articulating Spacer Technique for Infected Knee Arthroplasty?: A Preliminary Study. Clin Orthop Relat Res. 2012 Jan 1;470(1):228–35.

177. Jämsen E, Sheng P, Halonen P, Lehto MUK, Moilanen T, Pajamäki J, et al. Spacer prostheses in two-stage revision of infected knee arthroplasty. Int Orthop. 2006 Aug 1;30(4):257–61.

178. Masri BA, Duncan CP, Beauchamp CP. Long-term elution of antibiotics from bone-cement. J Arthroplasty. 1998 Apr 1;13(3):331–8.

179. Freeman MG, Fehring TK, Odum SM, Fehring K, Griffin WL, Mason JB. Functional Advantage of Articulating Versus Static Spacers in 2-Stage Revision for Total Knee Arthroplasty Infection. J Arthroplasty. 2007 Dec 1;22(8):1116–21.

180. Jiranek WA, Hanssen AD, Greenwald AS. Antibiotic-loaded bone cement for infection prophylaxis in total joint replacement. JBJS. 2006 Nov 1;88(11):2487-500.

181. Silvestre A, Almeida F, Renovell P, Morante E, López R. Revision of Infected Total Knee Arthroplasty: Two-Stage Reimplantation Using an Antibiotic-Impregnated Static Spacer. Clin Orthop Surg. 2013 Sep 1;5(3):180–7.

182. Kubista B, Hartzler RU, Wood CM, Osmon DR, Hanssen AD, Lewallen DG. Reinfection after two-stage revision for periprosthetic infection of total knee arthroplasty. Int Orthop. 2012 Jan 1;36(1):65–71.

183. Betsch BY, Eggli S, Siebenrock KA, Täuber MG, Mühlemann K. Treatment of Joint Prosthesis Infection in Accordance with Current Recommendations Improves Outcome. Clin Infect Dis. 2008 Apr 15;46(8):1221–6.

184. Mortazavi SMJ, Vegari D, Ho A, Zmistowski B, Parvizi J. Two-stage Exchange Arthroplasty for Infected Total Knee Arthroplasty: Predictors of Failure. Clin Orthop Relat Res. 2011 Nov 1;469(11):3049.

185. Hirakawa K, Stulberg BN, Wilde AH, Bauer TW, Secic M. Results of 2-stage reimplantation for infected total knee arthroplasty. J Arthroplasty. 1998 Jan 1;13(1):22–8.

186. Hofmann AA, Kane KR, Tkach TK, Plaster RL, Camargo MP. Treatment of infected total knee arthroplasty using an articulating spacer. Clinical orthopaedics and related research. 1995 Dec 1;321:45-54.

187. Berbari EF, Marculescu C, Sia I, Lahr BD, Hanssen AD, Steckelberg JM, et al. Culture-Negative Prosthetic Joint Infection. Clin Infect Dis. 2007 Nov 1;45(9):1113–9.

188. Fleck EE, Spangehl MJ, Rapuri VR, Beauchamp CP. An Articulating Antibiotic Spacer Controls Infection and Improves Pain and Function in a Degenerative Septic Hip. Clin Orthop Relat Res. 2011 Nov 1;469(11):3055–64.

189. Mortazavi SMJ, Vegari D, Ho A, Zmistowski B, Parvizi J. Two-stage exchange arthroplasty for infected total knee arthroplasty: predictors of failure. Clin Orthop. 2011 Nov;469(11):3049–54.

190. Hanssen AD, Rand JA, Osmon DR. Treatment of the infected total knee arthroplasty with insertion of another prosthesis: The effect of antibiotic-impregnated bone cement. Clinical orthopaedics and related research. 1994 Dec 1;309:44-55.

191. Zmistowski B, Tetreault MW, Alijanipour P, Chen AF, Della Valle CJ, Parvizi J. Recurrent Periprosthetic Joint Infection. J Arthroplasty. 2013 Oct 1;28(9):1486–9.

192. Sharma H, De Leeuw J, Rowley DI. Girdlestone resection arthroplasty following failed surgical procedures. International orthopaedics. 2005 Apr 1;29(2):92-5.

193. Castellanos J, Flores X, Llusà M, Chiriboga C, Navarro A. The Girdlestone pseudarthrosis in the treatment of infected hip replacements. Int Orthop. 1998 Jul 1;22(3):178–81.

194. Falahee MH, Matthews LS, Kaufer H. Resection arthroplasty as a salvage procedure for a knee with infection after a total arthroplasty. JBJS. 1987 Sep 1;69(7):1013-21.

195. Sierra RJ, Trousdale RT, Pagnano MW. Above-the-knee amputation after a total knee replacement: prevalence, etiology, and functional outcome. JBJS. 2003 Jun 1;85(6):1000-4.

196. Krijnen MR, Wuisman PIJM. Emergency hemipelvectomy as a result of uncontrolled infection after total hip arthroplasty. J Arthroplasty. 2004 Sep 1;19(6):803–8.

197. Hanssen AD, Trousdale RT, Osmon DR. Patient outcome with reinfection following reimplantation for the infected total knee arthroplasty. Clinical orthopaedics and related research. 1995 Dec 1;321:55-67.

198. Pavoni GL, Giannella M, Falcone M, Scorzolini L, Liberatore M, Carlesimo B, et al. Conservative medical therapy of prosthetic joint infections: retrospective analysis of an 8-year experience. Clin Microbiol Infect. 2004 Sep 1;10(9):831–7.

199. Byren I, Rege S, Campanaro E, Yankelev S, Anastasiou D, Kuropatkin G, et al. Randomized Controlled Trial of the Safety and Efficacy of Daptomycin versus Standard-of-Care Therapy for Management of Patients with Osteomyelitis Associated with Prosthetic Devices Undergoing Two-Stage Revision Arthroplasty. Antimicrob Agents Chemother. 2012 Nov 1;56(11):5626–32.

200. Rao N, Hamilton CW. Efficacy and safety of linezolid for Gram-positive orthopedic infections: a prospective case series. Diagn Microbiol Infect Dis. 2007 Oct 1;59(2):173–9.

201. Lin JC, Aung G, Thomas A, Jahng M, Johns S, Fierer J. The use of ceftaroline fosamil in methicillin-resistant Staphylococcus aureus endocarditis and deep-seated MRSA infections: a retrospective case series of 10 patients. J Infect Chemother. 2013 Feb 1;19(1):42–9.

# ANNEXURES

1. Patient information sheet
2. Consent forms
3. Clinical research form
4. Scores Used
5. IRB and Fluid Grant approval
6. Thesis Data

ANNEXURE I

**TITLE:** Outcome of Microbiologically Culture positive Arthroplasty Infections

Christian Medical College

**INFORMATION SHEET**

Periprosthetic joint infections, though not so common is a dreaded complication of joint replacement surgery. It leads to significant morbidity and also has a significant economic burden on the patient. It can lead to total failure of the implant resulting in revision surgeries and multiple other procedures.

We are trying to look at the organisms causing Periprosthetic joint infections and the change in the profile of organisms over the past decade.

**Why do we need to do the study?**

There has been a paradigm shift in the organisms that cause Periprosthetic joint infections. There is inadequate evidence of the same. This means that the antibiotic protocol might have to be modified to cover the newer organisms. Hence, we are looking at the changing trends in the organisms causing Periprosthetic joint infections.

**What will you have to do if you take part in this study?**

If you are taking part in this study, you need to consent for the same and your clinical records will be accessed from our registry. You will be subjected to routine blood tests and radiological investigations as a part of your regular follow up. No additional tests will be performed on you. You will be called back to assess the functional outcome.

**Are there any risks to participate in this study?**

There are no risks in the check up that will be done. The blood tests and X rays are a part of the regular follow up. Less than 10 ml of blood will be drawn and the X rays pose no added radiation risk.

**Can you withdraw from this study after it starts?**

Your participation in entirely voluntary, you are free to decide to withdraw permission to participate in this study. If you do so, this will not affect your treatment at CMC hospital

**Will I have to pay for the check up?**

The blood tests and X rays will be done free of cost.

**What happens when the study is over?**

When the study is over, we will give you the reports of the check up and the results. If you are found to have a condition that requires treatment or if you would benefit from a different antibiotic regimen, we will advise you regarding the same.

**Will my personal details be kept confidential?**

The results of this study will be published in a medical journal but you will not be identified by name. Your information may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any questions please contact Dr. Nirvin Paul [tel: 9952542591 or email nirvin.257@gmail.com]

**கிறிஸ்தவ மருத்துவக் கல்லூரி, வேலூர்**

**எலும்பு முறிவு சிகிச்சைப் பிரிவு**

தலைப்பு: மூட்டு அறுவைச் சிகிச்சைக்குப் பின்பாக உண்டாகும் தொற்றுக்களில் ஏற்படும் மாற்றங்களும் அதன் விளைவுகளும்.

**ஆய்வைக் குறித்த தகவல் தெரிவிக்கும் தாள் :**

செயற்கை மூட்டுத் தொற்று, மூட்டு மாற்று அறுவை சிகிச்சையிலே பயன்படுத்துகின்ற அளவிற்கு சிக்கல்களை ஏற்படுத்தாது. இது ஒரு குறிப்பிடத்தக்க அளவிலே நோயுற்ற நிலைமையையும், பணக் கஷ்டத்தையும் நோயாளிக்கு ஏற்படுத்தும். இது சில நேரங்களில் முழு தோல்வியை உண்டுபண்ணும், முழுவாக திரும்பவும் பலமுறை அறுவை சிகிச்சை செய்ய வேண்டியதாக இருக்கும்.

நாங்கள் இந்த செயற்கை மூட்டு தொற்று நோயை உண்டாக்குகின்ற பாக்டீரியாக்களையும் (அங்க ஜீவி) அதனால் ஏற்படுத்தப்படுகின்ற மாறுபாடுகளையும் கடந்த பத்து ஆண்டுகளாக கவனித்துக் கொண்டிருக்கின்றோம்.

**நாம் ஏன் இந்த ஆராய்ச்சி செய்ய வேண்டும்?**

ஒரு குறிப்பிடத்தக்க மாற்றங்கள் இந்த பாக்டீரியாக்களில் ஏற்படுவது செயற்கை மூட்டு தொற்று நோயை உண்டாக்குகின்றது. அதற்கான சான்றுகளும் குறைவானதாகவே உள்ளது. இந்த பாக்டீரியாக்களை அழிக்கக்கூடிய இரத்தத்தில் ஏற்கனவே உள்ள பொருள் புதிய பாக்டீரியாக்களை அழிக்கின்றது. இந்த பாக்டீரியாக்களின் மாறுபட்ட விதம் செயற்கை மூட்டு தொற்று நோயை உண்டாக்குகின்றது.

**இந்த ஆராய்ச்சியில் பங்கு பெற நீங்கள் என்ன செய்ய வேண்டும்?**

நீங்கள் இந்த ஆராய்ச்சியில் பங்கு பெற விரும்பினால் உங்களது மருத்துவப் பதிவேடுகள் மூலம் உங்களது மருத்துவக் குறிப்புகள் மதிப்பிடப்படும். உங்களைத் தொடர்ந்து பரிசோதிக்கும் விதமாக, இரத்தப் பரிசோதனை மற்றும் எக்ஸ்-ரே (கதிர்வீச்ச சிகிச்சை) போன்றவை எடுக்கப்படும். அதிகப்படியான சோதனைகள் எதுவும் செய்யப்படமாட்டாது என்பதையும் தெரிவிக்கின்றோம்.

**இந்த ஆராய்ச்சியில் பங்கு பெறுவதனால் ஏதாவது ஆபத்துகள் உண்டா?**

இந்தப் பரிசோதனைகளில் எந்த விதமான ஆபத்துகளும் இருப்பதில்லை. இரத்தப் பரிசோதனைகள் மற்றும் எக்ஸ்-ரே போன்றவைகள் உங்களது தொடர் பரிசோதனைகளில் ஒன்றாகும். 10 மில்லி லிட்டர் இரத்தத்தை விட குறைவானதாகவே இரத்தம் எடுக்கப்படும். எக்ஸ்-ரே எடுப்பதிலும் கதிர்வீச்சு அதிகமானதாக இருக்காது.

**நீங்கள் இந்த ஆராய்ச்சி ஆரம்பித்த பின்னர் இதிலிருந்து விலகிக் கொள்ள முடியுமா?**

நீங்கள் இதில் பங்கெடுப்பது முழுவதுமாக உங்களைச் சார்ந்தது. இந்த ஆராய்ச்சியில் இருந்து முழுவதுமாக விடுபட உங்களுக்கு உரிமை உண்டு. அப்படி நீங்கள் விடுபட்டால் அது நீங்கள் கிறிஸ்துவ மருத்துவக் கல்லூரியில் எடுத்துக் கொள்கின்றதான சிகிச்சையை எந்த விதத்திலும் பாதிக்காது.

**நான் இந்தப் பரிசோதனைகளுக்காகப் பணம் கட்ட வேண்டுமா?**

இந்த ஆய்விற்காகச் செய்யப்படும் இரத்தப் பரிசோதனைகளுக்கும், எக்ஸ்-ரேக்களுக்கும் நீங்கள் எவ்வித கட்டணமும் செலுத்தத் தேவையில்லை.

**இந்த ஆராய்ச்சி முடிந்த பின்னர் என்ன நடக்கும்?**

இந்த ஆராய்ச்சி முடிந்த பின்னர் நாங்கள் அதற்கான அறிக்கைகள் அதன் முடிவுகள் போன்றவற்றை உங்களுக்குத் தெரிவிப்போம். உங்களுக்கு சிகிச்சை தேவைப்பட்டாலோ அல்லது உங்களுக்கு கொடுக்கப்பட்டு வரும் நோய் எதிர்ப்பு மருந்தில் மாற்றம் தேவைப்பட்டாலோ அதை நாங்கள் பரிந்துரைப்போம்.

**என்னுடைய மருத்துவக் குறிப்புகள் இரகசியமாக வைக்கப்படுமா?**

இந்த ஆராய்ச்சியின் முடிவுகள் ஒரு மருத்துவப் புத்தகத்தில் வெளியிடப்படும். ஆனால், உங்களது பெயர் வெளியிடப்படமாட்டாது. உங்களது தகவல்கள் இந்த ஆராய்ச்சியில் சம்மந்தப்பட்டவர்களால் ஆராயப்படும். மேற்கண்ட தகவல்களின் அடிப்படையில் நீங்கள் இந்த ஆய்வில் பங்கேற்க விரும்பினால் ஒப்புதல் படிவத்தைப் பூர்த்தி செய்து, ஆய்வில் பங்கு பெறலாம்.

உங்களுக்கு ஏதாவது கேள்விகள் இருந்தால் தயவு செய்து **Dr. நிர்வின் பால்**, தொலைபேசி **9952542591** அல்லது மின்னஞ்சல்: **nirvin.257@gmail.com**-ஐத் தொடர்பு கொள்ளவும்.

**नकली जोड़ के आस पास होने वाले इन्फ़ेकशन मे बदलते दौर और उनके प्रवर्तियोन**

**क्रिशन मेडकल कोलेज**

## जानकारी पत्र

नकली जोड़ के आस पास होने वाले इन्फेकशन भले ही साधारण न हो लेकिन हडडे के जोड़ बदलने वाले चिकित्सा का खौफ़नाक कोम्प्लीकेशन है । इस के वजे से काफ़ी मौत होती है और पेशेंट पर भी काफ़ी आर्थिक दबाव पड़ जाता है । इस के वजेह से इम्प्ला पूरी तरह से नाकमयाब हो जाता है जिसके वजह से ओप्रेशन और काफ़ी सारी प्रक्रियान करनि पढती है ।

हम नकली जोड़ मे इन्फेकशन पेदा करने वाले किटाण और पिछले दस साल मे इन कीटण मे हुय बढ़ताव पर जाँच करने जा रहे है ।

**इस अधयन को करने की क्या ज़रूरत है?**

हडड के नकली जोड़ के आस पास होने वाले ईन्फेकशन को पेदा करने वाले कीटाण मे पीछले दस सालो में बड़ा बढ़ताव हुआ है । लेकिन इनके बारे मे हमारे पास जानकारी अधूरी है । इसका मतलब यह है कि इन कीटाण के लिये नये एनटीबायोटिक की ज़रूरत है. ईसलिय हम हद्दि के नक्लि जोद के आस पास होने वाले इन्फेक्शन को पेद करने वाले किटाणओ पर हम जाँच कर रहे है ।

**इस अधयन मे भाग लेने पर आपको क्या करना पढ़गा ?**

अगर आप इस अधयन मे भाग ले रहे है तो आपको इसके लिये सेहमती देनी पड़गी और आपकी जानकारी हम अपने पास रखे जानकारी से निकालेगे । जब आप अपने डाक्टर से मिलने आएगे तो सामानय तरीके से आपके खून की जाच और एक्स रे लिये जाएगे. इसके अलावा कुछ नया जाच नही करा जायेगा । आपको वापस बुलाया जयेगा

**क्या इस अधयन मै भाग लेने से कुछ हानी हो सकती है?**

करे जाने वाले जाचो से कुछ हानी नहीं होगी । खून के जाच और एक्स रे आपके सामन्य फौलो अप के ही भाग है । 10 से भी कम खून लीया जायेगा और एक्स रे से भी अलग रेडीएशन की हानी नही है ।

**इस अधयन के शूरू हो जाने के बाद इससे अपनी सेहमती वापस ले सकते है?**

आपका इस अधयन मे भाग लेना पूरी तरह से स्वेछिक है , इस मे भाग लेने की सेहमति वापस लेने के लिये आप पूरी तरह से आज़ाद है । एसा करने से सी एम सी मै आप के ईलाज पर कोई असर नही पडेगा ।

**क्या मुझे जाच के लिये पैसे भरने पड़ेगे?**

खून की जाच और एक्स रे मुफ़्त मै किये जायेगे ।

**अधयन खतम होने पर क्या होगा ?**

अधयन खतम होने पर हम आपको आपको आपके रीपोट देगे । अगर आपको और ईलाज या दूसरे एनटीबयोटीक की ज़रूरत है तो हम आपको इसके बारे मे सलाह देगे ।

**क्या मेरे निजी जानकारी गोपनीय रखी जायेगी?**

इस अधयन से मिले जानकारी को मेडीकल मेगज़ीन मै छापा जायेगा पर उस मे आपका नाम नही लीखा जायेगा । आपसे सेहमती लिये बिना, आपकी जानकारी इस अधयन से सम्बन्धित लोगो से पड़ जा सकती है अगर आप इस अधयन मे भाग लेने से अपनी सेहमती वापस लेना चाहे ।

अगर आपको कोइ सन्धय है तो आप इन से बात कर सकते है – डा. निर्वीन पाल ( फ़. नो 9952542591) या

ANNEXURE II

**Format for Informed Consent Form for Subjects**

Informed Consent form to participate in a research study

**Study Title:**

**Study Number: _____**

**Subject's Initials: _____ Subject's Name:**
**_____**

**Date of Birth / Age: _____**

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]

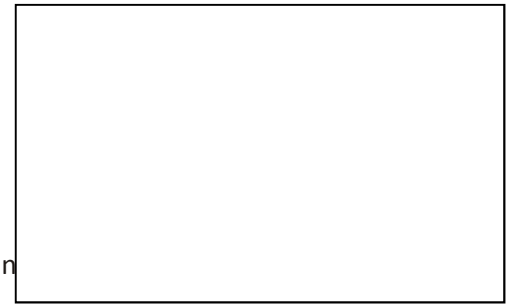
(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: _____/_____/_____

Signatory's Name: _____ Signature:

Or

Represen 

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature or thumb impression of the Witness: _____

Date: _____/_____/_____

Name & Address of the Witness: _____

---

இராய்ச்சியில் பங்கு பெறுபவர் பங்கு பெற ஒத்துக்கொள்ளும் ஒப்புதல் படிவம்

இராய்ச்சியின் தலைப்பு :

இராய்ச்சி ஏண்.:

இராய்ச்சியில் பங்குபெறுபவர்கள்

சுருக்கெழுத்து (ம) பெயர்:

பிறந்த தேதி / வயது:

i)மேலே இய்வு தேதியிட்ட தகவல் படிவத்தை நான் படித்து புரிந்துக் கொண்டேன். மேலும், கேள்விகள் கேட்க வாய்ப்பு கிடைத்தது ஏன்பதை ஊறுதி செய்கிறேன். [ ]

ii)ஈந்த இராச்சியில் ஏன்பங்கு தன்னார்வமே ஏன்பதை புரிந்துக்கொண்டு நான் ஏந்த நேரத்திலும், ஏந்த காரணத்தையும் சொல்லாமல், ஈந்த இராய்ச்சியிலிருந்து விலகினாலும் ஆது ஏன் மருத்துவ சிகிச்சையையோ ஆல்லது ஏனது சட்ட ஊரிமைகளையோ பாதிக்காது ஏன்பதை புரிந்துக் கொள்கிறேன். [ ]

iii)ஈந்த இய்வின் இதரவாளர்களோ, இதரவாளர்களின் சார்பில் ஈந்த இய்வில் பணிபுரிபவர்களையோ, கொள்கை குழுவினரோ மற்றும் மருத்துவ ஒழுங்கு நடவடிக்கை குழுவினரோ, ஏன்னுடைய மருத்துவ பதிவேட்டு விபரங்கள் ஈந்த இய்விற்காகவும், வருங்காலத்தில் ஐதேனும் இய்விற்காகவும் பயன்படுத்த ஏன் ஆனுமதியை பெற தேவையில்லை ஏன்பதையும், நான் ஈந்த இய்விலிருந்து விலகினாலும் ஏன்னிடமிருந்து, பெறப்பெற்ற குறிப்புகள் பயன்படுத்தி கொள்ளலாம் ஏன்றும் ஆறிந்துக் கொண்டேன். இனாலும், ஈந்த இய்வில் பயன்படுத்திய ஏன்னுடைய விவரங்கள் மூன்றாம் நபரிடமோ ஆல்லது ஒரு பதிப்பாகவோ வெளியிடும்போது ஏன்னுடைய ஆடையாளங்கள் நீக்கப்பட்டு விடும் ஏன்பதையும் நான் புரிந்துக் கொண்டேன். [ ]

iv)ஈந்த இய்வில் பயன்படுத்திய விவரங்கள் மற்றும் ஈந்த இய்வின் முடிவுகள் மருத்துவ ஆறிவியல் இராய்ச்சிக்காக பயன்படுத்துவதற்கு ஏவ்விதமான தடையுமில்லை ஏன ஒத்துக் கொள்கிறேன். [ ]

v)நான் மேலே குறிப்பிட்ட இய்வில் பங்கேற்க ஒப்புக்கொள்கிறேன். [ ]

கையொப்பம் ஆல்லது கைரேகை / சட்டப்படி ஐற்றுக்கொள்பவர்.

தேதி

கையொப்பமிடுபவர் பெயர் :  கையொப்பம் :

ஆல்லது.

பிரதிநிதி:

தேதி:

கையொப்பம்:

இராய்ச்சியாளரின் கையொப்பம்:

தேதி:

இராய்ச்சியாளரின் பெயர் :

சாட்சியாளரின் கையொப்பம் ஆல்லது கைரேகை:

தேதி:

சாட்சியாளரின் பெயர் மற்றும் விலாசம்:

विषय के बारे में बताए जाने का लिखित पत्र :.

- खोज की पढ़ाई में भाग लेने की जानकारी का पत्र

पढ़ाई का विषय :

पढ़ाई का नं. :

विषय का इनीशियल (पहला नाम):

विषय का नाम :

जन्म तिथि /आयु :

(विषय)

1) मैं आश्वासन देता/देती हूँ कि मैं दिए गए जानकारी के पत्र को समझा/समझी हूँ जो दी गई खोज की पढ़ाई के लिए की गई है और मुझे सवाल पूछने का पूरा मौका मिला।

2) मैं समझता/समझती हूँ कि इस पढ़ाई के लिए मेरा योगदान मेरी मरज़ी से दिया गया है और यह कि मैं इसमें भाग लेने से ~~बिना~~ बिना किसी तज़ुर्बा दिए कभी भी पीछे हट सकता/सकती हूँ। जिससे मेरे इलाज और कानूनी अधिकारों पर कोई प्रभाव नहीं नहीं पड़ेगा।

3) मैं समझता/समझती हूँ कि इस चिकित्सा प्रयास का करने वाला, इनकी जगह पर काम करने वाले लोग, अमीनी सरकारि और अधिकार रखने वालों को मेरे मेडिकल रिकॉर्ड देखने के लिए मेरी आज्ञा की

जरूरत नहीं होगी अभी की गई जाँच के बारे में भी और जो आगे की जाएँगी उनके बारे में भी।

चाहे मैं इसमें भाग लेने से बाहर निकल भी जाऊँ, मैं इस खोज से जुड़े लोगों को अपनी गुप्त जानकारियाँ जानने के बारे में हामि भरता हूँ।

और मैं ये जानता/जानती हूँ, कि मेरी पहचान किसी भी जानकारी में ज़ाहिर नहीं होगी और ना ही किसी तीसरे व्यक्ति को पता चलेगी।

4) मैं मानता/मानती हूँ कि आगे चलके अपने बारे में निकाली गई जानकारी का प्रयोग मैं हस्तेमाल करने से नहीं रोकूँगा/रोकूँगी। क्योंकि यह सिर्फ वैज्ञानिक कार्य के लिए है।

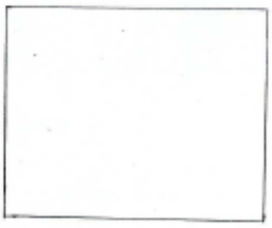
5) मैं ऊपर दी गई प्रयोग पढ़ाई में हिस्सा लेने के लिए हाँ करता/करती हूँ।

विषय का हस्ताक्षर/अंगूठे का निशान

दिनाँक __/__/__

हस्ताक्षर करने वाले का नाम

हस्ताक्षर



प्रतिनिधित्व : _____

दिनाँक : __/__/__

हस्ताक्षर करने वाले का नाम : _____

खोजी के हस्ताक्षर : _____

दिनाँक __/__/__

पसंद के खोजी का नाम : _____

गवाह का हस्ताक्षर या अंगूठे का निशान : _____

दिनाँक __/__/__

गवाह का नाम और पता : _____

_____

## গবেষণায় অংশগ্রহণের জন্য সম্মতি পত্র :

গবেষণার নাম : _____

গবেষণার নম্বর : _____

অংশগ্রহণকারীর স্বাক্ষর : _____

অংশগ্রহণকারীর নাম : _____

জন্মতারিখ / বয়স : _____

(অংশগ্রহণকারী)

ক) আমি জানাচ্ছি যে আমি পড়েছি এবং বুঝেছি উপরে , যার তারিখ ছিল _____ , উল্লেখিত গবেষণার জন্য এবং প্রশ্ন জিজ্ঞাসা করার সুযোগ পেয়েছি। [ ]

খ) আমি বুঝেছি যে এই গবেষণায় অংশগ্রহণ করা সম্পূর্ণ আমার ইচ্ছা এবং যে কোন মুহূর্তে আমি এই গবেষণা থেকে আমার সম্মতি তুলে নিতে পারি, কোন কারণ ছাড়া। এতে আমার চিকিৎসা অথবা আমার আইনত অধিকার কোন ভাবে প্রভাবিত হবে না।

গ) আমি বুঝেছি যে এই গবেষণার ফলাফল এবং যারা ফলাফলের হয়ে কাজ করছে, নিয়ামক মন্ডলী ও পরিচালনা সমিতি আমার সম্মতি ছাড়াই আমার গুরুত্বপূর্ণ তথ্য দেখবে যাতে আমার চলমান তথ্য

৩ গবেষণার তথ্য থাকবে, যদিও আমি এই গবেষণা থেকে আপনার অংশগ্রহণ তুলে নি, আমি এই বিষয়ে আপনার অনুমতি দিচ্ছি। কিন্তু আমি এটাও বুঝেছি যে আপনার পরিচিতি কোন তৃতীয় ব্যক্তি কাছে প্রকাশিত হবে না। [ ]

৪) আমি আপনার ব্যক্তিগত তথ্য ব্যবহারের জন্য অনুমতি দিচ্ছি যদি তেমন কোন বৈজ্ঞানিক কাজের জন্য ব্যবহৃত হয়।

৫) আমি উল্লেখিত গবেষণায় অংশগ্রহণের জন্য অনুমতি দিলাম।

স্বাক্ষর / আঙুলের ছাপ যা আবশ্যিক প্রযোজ্য:

_____

তারিখ : _____/_____/_____

ডিসলেটরীর নাম : _____

স্বাক্ষর : _____ বা

তথ্যপ্রদানকারীর স্বাক্ষর : _____

তারিখ : _____/_____/_____

ডিসলেটরির নাম: _____

গবেষকের স্বাক্ষর : _____

তারিখ : _____/_____/_____

গবেষণার তথ্য সংগ্রাহকের নাম: _____

স্বাক্ষীর আঙুলের ছাপ অথবা স্বাক্ষর : _____

তারিখ : _____/_____/_____

স্বাক্ষীর নাম ও ঠিকানা : _____

ANNEXURE III

Proforma

***STUDY TITLE:***

OUTCOME OF MICROBIOLOGICALLY CULTURE PROVEN INFECTED ARTHROPLASTIES

PATIENT ID:

NAME :

HOSPITAL NUMBER:

AGE:

SEX:(M/F)

OCCUPATION:

RELIGION:

ADDRESS:

DATE OF DATA ENTRY:

PHONE NUMBER:

EMAIL :

*ADMISSION DETAILS*

DATE OF ADMISSION:

DATE OF DISCHARGE:

WARD:
UNIT:

CO MORBID ILLNESS:

*PREVIOUS ARTHROPLASTY DETAILS*

HIP OR KNEE ARTHROPLASTY:

IMPLANT USED:

DATE OF THE SURGERY:

DURATION SINCE SURGERY:

HOSPITAL WHERE SURGERY WAS DONE:

CHIEF COMPLAINS:

*PREOPERATIVE INVESTIGATION RESULTS*

SINUS PRESENT OR ABSENT:

TOTAL LEUCOCYTE COUNT:

NEUTROPHIL COUNT:

E.S.R:

C.R.P:

SYNOVIAL TOTAL WBC COUNT:

SYNOVIAL NEUTROPHIL COUNT:

LEUCOCYTE ESTERASE TEST:

*INTRAOPERATIVE INVESTIGATION RESULTS*

S.NO ORGANISM(S) SENSTIVITY

CULTURE :I)

II)

III)

HISTOPATHOLOGY: NUMBER OF NEUTROPHILS/HIGH POWER FIELD:

SYNOVIAL FLUID ANALYSIS:

i) TLC
ii) PMN%

PRESCENCE OF PURULENCE:

DURATION OF HOSPITALISATION:

ANTIBIOTIC RECEIVED:

DURATION:

FINAL OUTCOME OF PROSTHESIS:

MODIFIED HARRIS HIP SCORE:

NEW OXFORD KNEE SCORE:

## ANNEXURE IV

**NEW OXFORD KNEE SCORE QUESTIONNAIRE**

Please answer the following 12 questions. Choose only one answer per question. The value for each answer is indicated to the right of the answer. Total up all of your answers to obtain a total score out of 48 points. Please only consider how you have been getting on during the past four weeks

| | |
|---|---|
| **Name:** | |
| **Date:** | |
| **Left or right Knee?** | |

| | | Score |
|---|---|---|
| . | **How would you describe the pain you have usually from your knee?**<br>None – **4**<br>Very mild – **3**<br>Mild – **2**<br>Mild moderate – **1**<br>Severe – **0** | |
| . | **Have you had any trouble with washing and drying yourself all over because of your knee?**<br>No trouble at all – **4**<br>Very little trouble – **3**<br>Moderate trouble – **2**<br>Extreme difficulty – **1**<br>Impossible to do – **0** | |
| . | **Have you had any trouble getting in and out of a car or using public transport because of your knee?**<br>No trouble at all – **4**<br>Very little trouble – **3**<br>Moderate trouble – **2**<br>Extreme difficulty – **1**<br>Impossible to do – **0** | |
| . | **If you were to kneel down could you stand up afterwards?**<br>Yes, easily – **4**<br>With little difficulty – **3**<br>With moderate difficulty – **2**<br>With extreme difficulty – **1**<br>No, impossible – **0** | |

| | | Score |
|---|---|---|
| 8. | **Have you been able to do your own household shopping on your own?**<br>Yes, easily – **4**<br>With little difficulty – **3**<br>With moderate difficulty – **2**<br>With extreme difficulty – **1**<br>No, impossible – **0** | |
| 9. | **For how long have you been able to walk before the pain from your knee became severe (with or without a stick)?**<br>No pain, even after more than 30 minutes – **4**<br>16-30 minutes – **3**<br>5-15 minutes – **2**<br>Around the house only – **1**<br>Unable to walk at all – **0** | |
| 10. | **Have you been able to walk down a flight of stairs**<br>Yes, easily – **4**<br>With little difficulty – **3**<br>With moderate difficulty – **2**<br>With extreme difficulty – **1**<br>No, impossible – **0** | |
| 11. | **After a meal (sat at a table) how painful has it been for you to stand up from a chair because of your knee?**<br>Not at all painful – **4**<br>Slightly painful – **3**<br>Moderately painful – **2**<br>Very painful – **1**<br>Unbearable – **0** | |

. **Have you been limping when walking because of your knee?**

Rarely/never – **4**
Sometimes or just at first – **3**
Often, not just at first – **2**
Most of the time – **1**
All of the time – **0**

. **Have you felt that your knee might suddenly give way or let you down?**

Rarely/never – **4**
Sometimes or just at first – **3**
Often, not just at first – **2**
Most of the time – **1**
All of the time – **0**

12. **How much pain from your knee interfered with your usual work (including housework)?**

Not at all – **4**
A little bit – **3**
Moderately – **2**
Greatly – **1**
Totally – **0**

13. **Have you been troubled by pain from your knee in bed at night?**

No nights – **4**
Only 1 or 2 nights – **3**
Some nights – **2**
Most nights – **1**
Every night – **0**

**TOTAL SCORE: /48**

## Modified Harris Hip Score

***Please mark one choice for each topic:***

Pain:
___None/ignores (44points)
___Slight, occasional, no compromise in activity (40 points)
___Mild, no effect on ordinary activity, pain after activity, uses aspirin (30 points)
___Moderate, tolerable, makes concessions, occasional codeine (20 points)
___Marked, serious limitations (10 points)
___Totally disabled (0 points)

Function: Gait
Limp
___None (11 points)
___Slight (8 points)
___Moderate (5 points)
___Severe (0 points)
___Unable to walk (0 points)

Support
___None (11 points)
___Cane, long walks (7 points)
___Cane, full time (5 points)
___Crutch (4 points)
___2 canes (2 points)
___2 crutches (1 points)
___Unable to walk (0 points)

Distance Walked
___Unlimited (11 points)
___6 blocks (8 points)
___2-3 blocks (5 points)
___Indoors only (2 points)
___Bed and chair (0 points)

Functional Activities:
Stairs
___Normally (4 points)
___Normally with banister (2 points)
___Any method (1 points)
___Not able (0 points)

Socks/Shoes
___With ease (4 points)
___With difficulty (2 points)
___Unable (0 points)

Sitting
___Any chair, 1 hour (5 points)
___High chair, ½ hour (3 points)
___Unable to sit, ½ hour, any chair (0 points)

Public Transportation
___Able to enter public transportation (1 points)
___Unable to use public transportation (0 points)

ANNEXURE V

**OFFICE OF RESEARCH**
**INSTITUTIONAL REVIEW BOARD (IRB)**
**CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA**

**Dr. B.J. Prashantham,** M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

**Dr. Alfred Job Daniel,** D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

**Dr. Biju George,** MBBS., MD., DM
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

June 20, 2016

Dr. Nirvin Paul ,
PG Registrar,
Department of Orthopaedics,
Christian Medical College,
Vellore 632 004.

Sub: **Fluid Research Funding: New Proposal**
Outcome of Microbiological culture Positive Arthroplasty Infections
Nirvin Paul (Employment Number: 29469), Post graduate Registrar, Orthopaedics, Dr. Alfred Job Daniel Employment Number: 11140, Orthopaedics III, Dr. PRJVC Boopalan, Emp No.: 28326, Orthopaedics III, Dr. John Antony Jude Prakash (Emp No.: 14982), Microbiology, Dr. Balaji V, (Emp No.: 30033), Microbiology,

Ref: IRB Min No: 9922 [OTHER] dated 05.02.2016

Dear Dr. Nirvin Paul,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Cc: Dr. Alfred Job Daniel, Department of Orthopaedics, CMC



Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

**OFFICE OF RESEARCH**
**INSTITUTIONAL REVIEW BOARD (IRB)**
**CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA**

**Dr. B.J. Prashantham,** M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

**Dr. Alfred Job Daniel,** D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

**Dr. Biju George,** MBBS., MD., DM
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

June 20, 2016

Dr. Nirvin Paul ,
PG Registrar,
Department of Orthopaedics,
Christian Medical College,
Vellore 632 004.

Sub: **Fluid Research Funding: New Proposal**
Outcome of Microbiological culture Positive Arthroplasty Infections
Nirvin Paul (Employment Number: 29469), Post graduate Registrar, Orthopaedics, Dr. Alfred Job Daniel Employment Number: 11140, Orthopaedics III, Dr. PRJVC Boopalan, Emp No.: 28326, Orthopaedics III, Dr. John Antony Jude Prakash (Emp No.: 14982), Microbiology, Dr. Balaji V, (Emp No.: 30033), Microbiology,

Ref: IRB Min No: 9922 [OTHER] dated 05.02.2016

Dear Dr. Nirvin Paul

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Outcome of Microbiological culture Positive Arthroplasty Infections" on February 05th 2016.

The Committee reviewed the following documents:

1. IRB Application format
2. Patient Information Sheet and Informed Consent Form (English, Tamil, Hindi, Bengali)
3. Modified Harris Hip Score(English, Tamil, Hindi, Bengali)
4. NEW OXFORD KNEE SCORE QUESTIONNAIRE(English, Tamil, Hindi, Bengali)
5. Cvs of Drs. Nirvin Paul , PRJVC Boopalan, Alfred Job Daniel, John Antony Jude Prakash, Balaji V,
6. No. of documents 1 - 5

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on February 05th 2016 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.



Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

**Dr. B.J. Prashantham,** M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

**Dr. Alfred Job Daniel,** D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

**Dr. Biju George,** MBBS., MD., DM
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

| Name | Qualification | Designation | Affiliation |
|---|---|---|---|
| Dr. Biju George | MBBS, MD, DM | Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC,Vellore | Internal, Clinician |
| Dr. Nihal Thomas | MD, MNAMS, DNB (Endo), FRACP (Endo) FRCP(Edin) FRCP (Glasg) | Professor & Head, Endocrinology. CMC, Vellore | Internal, Clinician |
| Dr. Jayaprakash Muliyil | BSc, MBBS, MD, MPH, Dr PH (Epid), DMHC | Retired Professor, Vellore | External, Scientist &Epidemiologist |
| Rev. Joseph Devaraj | BSc, BD | Chaplaincy Department, CMC, Vellore | Internal, Social Scientist |
| Dr. Balamugesh | MBBS, MD(Int Med), DM, FCCP (USA) | Professor, Pulmonary Medicine, CMC, Vellore | Internal, Clinician |
| Dr. Visalakshi. J | MPH, PhD | Lecturer, Biostatistics, CMC, Vellore | Internal, Statistician |
| Mrs. Sheela Durai | MSc Nursing | Professor, Medical Surgical Nursing, CMC, Vellore | Internal, Nurse |
| Dr. Niranjan Thomas | DCH, MD, DNB (Paediatrics) | Professor, Neonatology, CMC, Vellore | Internal, Clinician |
| Mrs. Pattabiraman | BSc, DSSA | Social Worker, Vellore | External, Lay Person |
| Dr. B. J. Prashantham | MA(Counseling Psychol MA(Theology), Dr. Min(Clinical Counselling) | Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centr Vellore | External, Social Scientist |
| Dr. RatnaPrabha | MBBS, MD (Pharma) | Associate Professor, Clinical Pharmacology, CMC, Vellore | Internal, Pharmacologist |



Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

**Dr. B.J. Prashantham,** M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

**Dr. Alfred Job Daniel,** D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

**Dr. Biju George,** MBBS., MD., DM
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

| | | | |
|---|---|---|---|
| Mrs. Emily Daniel | MSc Nursing | Professor, Medical Surgical Nursing, CMC, Vellore | Internal, Nurse |
| Dr. Vivek Mathew | MD (Gen. Med.) DM (Neuro) Dip. NB (Neuro) | Professor, Neurology, CMC, Vellore | Internal, Clinician |
| Mr. C. Sampath | BSc, BL | Advocate, Vellore | External, Legal Expert |
| Dr. Inian Samarasam | MS, FRCS, FRACS | Professor, Surgery, CMC, Vellore | Internal, Clinician |

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "Outcome of Microbiological culture Positive Arthroplasty Infections" on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in)

*Fluid Grant Allocation:*

*A sum of 44,800/- INR (Rupees Forty four thousand eight hundred Only) will be granted for 3 years.*

Yours sincerely

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

IRB Min No: 9922 [OTHER] dated 05.02.2016 4 of 4



ANNEXURE VI

| Serial numl | Name | Hosp no | age | gender | religion | no of admi | duration | unit | Co morbid | co morbid : | co morbid : | co morbid - | joint |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 3 | Anup Kum | 344605f | 55 | 1 | 1 | 1 | 13 | 3 | 1 | | | | 1 |
| 1 | Mohamma | 191181d | 55 | 1 | 2 | 2 | 36 | 2 | | 8 | 9 | | 2 |
| 2 | Bharati C | 022611c | 57 | 2 | 1 | 1 | 23 | 3 | 7 | 3 | | | 1 |
| 4 | Usha Devi | 820811f | 57 | 2 | 1 | 1 | 16 | 3 | 2 | | | | 2 |
| 5 | Jayant Kur | 683209d | 51 | 1 | 1 | 4 | 63 | 1 | | | | | 1 |
| 6 | Utpal Dutt | 996835d | 32 | 1 | 1 | 3 | 37 | 1 | | | | | 1 |
| 7 | Sharadamr | 702399c | 71 | 2 | 1 | 3 | 68 | 2 | 1 | 2 | | | 1 |
| 8 | Noor Moh | 450261f | 75 | 1 | 2 | 1 | 17 | 1 | 1 | 2 | 4 | | 1 |
| 9 | Ekambaran | 906379c | 46 | 1 | 1 | 4 | 40 | 3 | 10 | | | | 1 |
| 10 | Sumti Kum | 562051c | 66 | 1 | 1 | 2 | 25 | 1 | 4 | 9 | | | 1 |
| 11 | Sabita Rani | 031434g | 53 | 2 | 1 | 1 | 39 | 1 | 1 | 2 | | | 2 |
| 12 | John Kenn | 301527d | 52 | 1 | 3 | 1 | 14 | 3 | 1 | | | | 1 |
| 13 | Chinnaiyan | 202627f | 67 | 1 | 1 | 3 | 30 | 3 | | | | | 1 |
| 14 | Dominic Bc | 157474c | 50 | 1 | 3 | 1 | 12 | 2 | 2 | 7 | | | 1 |
| 15 | Sundarraj | 564980g | 33 | 1 | 1 | 1 | 12 | 2 | | | | | 1 |
| 16 | Chandrawa | 704760c | 66 | 2 | 1 | 2 | 19 | 3 | | | | | 2 |
| 17 | Haobam Ja | 679074d | 54 | 1 | 1 | 4 | 79 | 1 | | | | | 2 |
| 18 | Dr.Nagasur | 462980f | 65 | 2 | 1 | 2 | 42 | 1 | 2 | 5 | 8 | 7 | 2 |
| 19 | Ashesha Na | 830828b | 44 | 1 | 1 | 2 | 33 | 3 | 1 | 2 | 6 | 7 | 1 |
| 20 | Rita Sahu | 976250d | 57 | 2 | 1 | 4 | 68 | 3 | 1 | 5 | | | 1 |
| 21 | Shanti Ksh | 863002f | 62 | 2 | 1 | 2 | 56 | 1 | | | | | 1 |
| 22 | Annammal | 350008a | 82 | 2 | 3 | 4 | 126 | 2 | 2 | 8 | | | 2 |
| 23 | Nirmal Ghc | 991774g | 38 | 1 | 1 | 2 | 24 | 2 | | | | | 1 |
| 24 | Sivalingam | 014526d | 66 | 1 | 1 | 1 | 8 | 3 | 2 | | | | 2 |

| type of hip | cemented | year of sur | duration sir | index | Chie co 1 | chie 2 | chief co 3 | chief 4 | sinus | Pre TC | Pre PMN | Pre ESR | pre CRP |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 2 | 2 | 37 | 1 | 1 | | | | 2 | | | 5 | 3.19 |
| | | 1 | 95 | 1 | 2 | 1 | 4 | | 1 | 7100 | 61 | 16 | 9.78 |
| 1 | 2 | 1 | 85 | 1 | 2 | | | | 2 | 5200 | 69 | 95 | 14.1 |
| | | 2 | 35 | 1 | 1 | | | | 2 | | | 66 | 42.1 |
| 2 | 1 | 1 | 90 | 2 | 1 | 2 | | | 1 | | | 24 | 63.8 |
| 2 | 2 | 2 | 58 | 2 | 1 | | | | 2 | 6300 | 60 | 41 | 8.99 |
| 2 | 1 | 2 | 36 | 1 | 2 | 1 | 5 | | 2 | 9300 | 72 | 47 | 8.71 |
| 2 | 2 | 2 | 48 | 2 | 1 | 4 | | | 2 | 6100 | 68 | | |
| 1 | 2 | 1 | 120 | 1 | 2 | 1 | | | 1 | 10300 | 77 | 71 | 65.3 |
| 4 | 2 | 2 | 45 | 1 | 1 | | | | 2 | | | 5 | 3.19 |
| | | 2 | 33 | 1 | 1 | | | | 2 | | | 38 | |
| 1 | 2 | 1 | 104 | 1 | 1 | 2 | 4 | | 2 | | | 20 | 3.19 |
| 4 | 1 | 2 | 60 | 2 | 1 | 4 | | | 2 | | | 45 | 20.2 |
| 4 | 2 | 2 | 38 | 1 | 1 | | | | 2 | 7560 | 65 | 56 | 7.61 |
| 1 | 2 | 2 | 40 | 2 | 1 | 4 | | | 2 | 11400 | 64 | 3 | 113 |
| | | 1 | 116 | 1 | 1 | | | | 2 | 13800 | 73 | | 178 |
| | | 1 | 87 | 1 | 1 | 2 | 4 | | 1 | 6700 | 78 | 44 | 28 |
| | | 1 | 120 | 2 | 1 | 2 | 3 | 5 | 2 | 12700 | 83 | 80 | 118 |
| 1 | 2 | 1 | 124 | 1 | 1 | 4 | | | 2 | | | 65 | 70.8 |
| 2 | 2 | 2 | 73 | 2 | 2 | 1 | | | 1 | 8400 | 52 | 55 | 6.65 |
| 4 | 2 | 2 | 39 | 1 | 1 | 2 | | | 1 | 7300 | 66 | 21 | 3.45 |
| | | 2 | 42 | 1 | 1 | 2 | 4 | | 1 | 12900 | 70 | 47 | 25.8 |
| 1 | 2 | 2 | 34 | 2 | 1 | 4 | | | 2 | 13500 | 77 | 51 | 62.6 |
| | | 2 | 44 | 1 | 1 | 5 | | | 2 | 2400 | 76 | 45 | 443 |

| Pre syno TC | pre syno PI | Cul 1 | staph sens | Sens GNB 1 | Sens CONS | Cul 2 | sens stap 2 | sens gnb 2 | sens cons 2 | cul 3 | sens staph | sens GNB 3 | sens cons 3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 1 | | | | | | | | | | |
| 5800 | 5510 | 1 | 1 | | | | | | | | | | |
| | | 5 | | | | | | | | | | | |
| | | 1 | 1 | | | | | | | | | | |
| | | 1 | 2 | | | | 2 | | 1 | | | | |
| | | 3 | | | 1 | | | | | | | | |
| | | 2 | | 1 | | | 2 | | 1 | | 2 | 1 | |
| | | 5 | | | | | 5 | | | | | | |
| | | 1 | 1 | | | | 1 | 1 | | | 3 | | 1 |
| | | 3 | | | 1 | | | | | | | | |
| | | 3 | | | 1 | | | | | | | | |
| | | 3 | | | 1 | | | | | | | | |
| | | 3 | | | 1 | | 3 | | | 1 | | | |
| | | 5 | | | | | | | | | | | |
| | | 2 | | 1 | | | | | | | | | |
| | | 3 | | | 2 | | | | | | | | |
| | | 1 | 2 | | | | 1 | 2 | | | 1 | 2 | |
| 9800 | 98 | 4 | | | | | 2 | | 1 | | 2 | 1 | |
| | | 5 | | | | | 1 | 1 | | | 1 | 2 | |
| | | 2 | | 1 | | | 2 | | 1 | | 2 | 1 | |
| | | 2 | | 3 | | | | | | | | | |
| 18000 | 98 | 1 | 2 | | | | 1 | 2 | | | | | |
| | | 1 | 1 | | | | | | | | | | |
| | | 6 | | | | | 6 | | | | | | |

| int syn tc | int syn PMI | pus | HPE | ABX 1 | Weeks 1 | | ABX 2 | Weeks 2 | | ABX 3 | Weeks 3 | | final outcol | lat esr | lat TC | lat PMN |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 3 | 2 | 6 | 4 | 5 | 4 | | | 1 | 8 | 5600 | 53 |
| 30 | 31 | | 2 | 1 | 3 | 6 | 6 | 12 | | | | | 3 | 30 | 6300 | 59 |
| | | | | | 14 | 4 | | | | | | | 1 | 58 | 4300 | 58 |
| | | | | | 6 | 6 | 13 | 6 | | | | | 1 | 34 | 9400 | 72 |
| | | | 1 | | 3 | 6 | | | | | | | 6 | 2 | 9300 | 71 |
| | | | | | 3 | 6 | | | | | | | 3 | 3 | | |
| | | | 1 | | 7 | 6 | | | | | | | 7 | 108 | 7900 | 92 |
| | | | | | 6 | 2 | 2 | 4 | | | | | 2 | 14 | 7000 | 69 |
| | | | 1 | 1 | 6 | 12 | 5 | 8 | | | | | 6 | 23 | 10600 | 76 |
| | | | 2 | | 4 | 2 | 2 | 3 | | | | | 1 | 4 | 6400 | 61 |
| | | | | | 3 | 4 | | | | | | | 1 | 21 | | |
| | | | | | 5 | 6 | | | | | | | 1 | 3 | 7500 | 53 |
| | | | | | 6 | 6 | | | | | | | 3 | 6 | 4100 | 45 |
| | | | | | 6 | 6 | 1 | 6 | | | | | 2 | 24 | 6600 | 59 |
| | | | 2 | 2 | 15 | 6 | 16 | 6 | | | | | 3 | 64 | 9400 | 73 |
| | | | | | 1 | 4 | 8 | 4 | | | | | 1 | 48 | | |
| | | | 1 | | 6 | 4 | 5 | 12 | 1 | 12 | | | 3 | 20 | 10200 | 82 |
| 131920 | 70 | | 1 | 1 | 10 | 468 | 4 | 4 | 16 | 8 | | | 5 | 44 | 10100 | 77 |
| | | | | | 1 | 4 | | | | | | | 1 | 105 | | |
| | | | | | 9 | 2 | 5 | 10 | 12 | 2 | | | 6 | 60 | | |
| | | | | | 4 | 2 | 2 | 2 | 5 | 8 | | | 1 | 45 | | |
| | | | | | 1 | 4 | 3 | 6 | 15 | 8 | | | 3 | 70 | | |
| | | | | | 3 | 6 | 6 | 6 | | | | | 3 | | | |
| | | | | | 4 | 2 | | | | | | | 7 | | | |

| Lat CRP | Xray | Now sinus | NOKS | MHHS |
|---|---|---|---|---|
| 3.17 | 2 | 2 | | 76 |
| 3.48 | 2 | 1 | 17 | |
| 21.6 | 2 | 2 | | 78 |
| 7.08 | 2 | | 36 | |
| 3.02 | | 1 | | 78 |
| 3.02 | 2 | 2 | | 82 |
| 31.4 | 1 | 1 | | 0 |
| 2.13 | 2 | 2 | | 65 |
| 5.44 | | 2 | | 85 |
| 3.57 | 2 | 2 | | 74 |
| 1.04 | 2 | 2 | 47 | |
| 3.02 | 2 | 2 | | 91 |
| 3.02 | 2 | 2 | | 26 |
| 3.03 | 1 | 2 | | 66 |
| 37.5 | | 2 | | 8 |
| 3.24 | 2 | 2 | 37 | |
| 33.7 | 1 | 1 | 24 | |
| 11.5 | | 2 | 4 | |
| 15 | 2 | 2 | | 17 |
| 12.3 | | 2 | | 67 |
| 1.8 | 1 | 2 | | 80 |
| 10.8 | 2 | 2 | 38 | |
| | | | | 26 |